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=> fil reg; d stat que l18; fil capl; d que nos l19; fil uspat; d que nos l20 FILE 'REGISTRY' ENTERED AT 11:50:16 ON 19 SEP 2001
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Liu

STRUCTURE FILE UPDATES: 18 SEP 2001 HIGHEST RN 357383-23-4 DICTIONARY FILE UPDATES: 18 SEP 2001 HIGHEST RN 357383-23-4

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

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Structure search limits have been increased. See HELP SLIMIT for details.

L7 -	STR		= ring or chain bonds & nodes
A 9 2 G1 > Pt > Hy 3	H2N√^Ak @4 5	Ak-✓NH ✓ Ak 6 @7 8	A = any non-hydrogen atom
Â A 10			

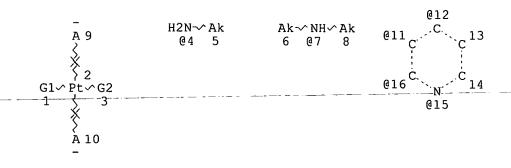
93 nodes 9810 carry any negative charge VAR G1=NH3/4/7 NODE ATTRIBUTES: CHARGE IS *-CHARGE IS *-ΑT NSPEC IS RC AΤ NSPEC IS RC ΑT NSPEC IS RC 10 ΑT full file search done on this structure CONNECT IS E1 5 RC AT CONNECT IS E1 RC AT 6 CONNECT IS E1 RC AT DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L9 327 SEA FILE=REGISTRY SSS FUL L7

L11 STR



VAR G1=NH3/4/7 VAR G2=15/16/11/12 NODE ATTRIBUTES: IS *-CHARGE CHARGE IS *-AT 10 IS RC .NSPEC AT 2 IS RC NSPEC AT IS RC NSPEC AT 10 CONNECT IS E1 RC AT 5 CONNECT IS E1 RC AT 6 CONNECT IS E1 RC AT DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED subset search done
"NOT"-ing out this structure
('Z is other than pyridine")

GRAPH ATTRIBUTES:

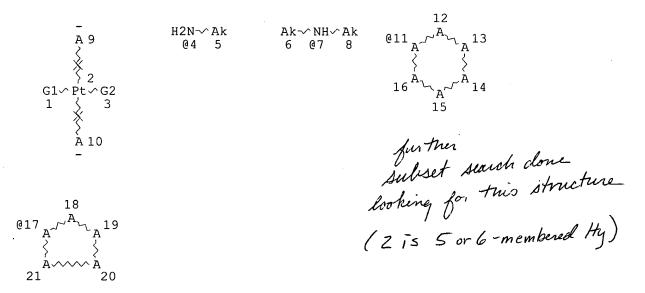
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L13 157 SEA FILE=REGISTRY SUB=L9 SSS FUL L11 L14 170 SEA FILE=REGISTRY ABB=ON L9 NOT L13

L16 STR



VAR G1=NH3/4/7 VAR G2=11/17 NODE ATTRIBUTES:

9 CHARGE IS *-ΑT CHARGE IS *~ AT10 NSPEC IS RC AΤ 2 IS RC. AΤ 9 NSPEC IS RC 10 NSPEC ΑT 5 CONNECT IS E1 RC AT CONNECT IS E1 RC AT 6 CONNECT IS E1 RC AT DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 11 17

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L18 119 SEA FILE=REGISTRY SUB=L14 SSS FUL L16

100.0% PROCESSED 169 ITERATIONS

119 ANSWERS

SEARCH TIME: 00.00.05

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FILE COVERS 1947 - 19 Sep 2001 VOL 135 ISS 13 FILE LAST UPDATED: 18 Sep 2001 (20010918/ED)

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L9 327 SEA FILE=REGISTRY SSS FUL L7
L11 STR
L13 157 SEA FILE=REGISTRY SUB=L9 SSS FUL L11
L14 170 SEA FILE=REGISTRY ABB=ON L9 NOT L13
L16 STR
L18 119 SEA FILE=REGISTRY SUB=L14 SSS FUL L16
L19 55 SEA FILE=CAPLUS ABB=ON L18
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FILE 'USPATFULL' ENTERED AT 11:50:18 ON 19 SEP 2001 CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Sep 2001 (20010918/PD)
FILE LAST UPDATED: 18 Sep 2001 (20010918/ED)
HIGHEST GRANTED PATENT NUMBER: US6292944
HIGHEST APPLICATION PUBLICATION NUMBER: US2001016957
CA INDEXING IS CURRENT THROUGH 18 Sep 2001 (20010918/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Sep 2001 (20010918/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2001
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2001

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 >>> and applications are typically loaded on the day of publication.<<<
 >>> Page images are available for display by the following day. <<<
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- >>> Complete CA file indexing for chemical patents (or equivalents) <<< >>> is included in file records. A thesaurus is available for the >>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<< >>> fields. This thesaurus includes catchword terms from the <<< >>> USPTO/MOC subject headings and subheadings. Thesauri are also <<< >>> available for the WIPO International Patent Classification <<< >>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<< >>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<< >>> the /IC5 and /IC fields include the corresponding catchword <<< >>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L7
                STR
L9
            327 SEA FILE=REGISTRY SSS FUL L7
L11
                STR
L13
            157 SEA FILE=REGISTRY SUB=L9 SSS FUL L11
            170 SEA FILE=REGISTRY ABB=ON L9 NOT L13
L14
L16
                STR
L18
            119 SEA FILE=REGISTRY SUB=L14 SSS FUL L16
T.20
              9 SEA FILE=USPATFULL ABB=ON L18
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=> dup rem 119,120

FILE 'CAPLUS' ENTERED AT 11:50:25 ON 19 SEP 2001

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PROCESSING COMPLETED FOR L20

L22 63 DUP REM L19 L20 (1 DUPLICATE REMOVED)

ANSWERS '1-55' FROM FILE CAPLUS ANSWERS '56-63' FROM FILE USPATFULL

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ANSWER 1 OF 63 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1

ACCESSION NUMBER: 1997:311254 CAPLUS

DOCUMENT NUMBER: 126:350803

TITLE: <u>Trans-pl</u>atinum(IV) complexes containing at least one

heterocyclic planar ligand as antitumor agents

INVENTOR(S): Farrell, Nicholas

PATENT ASSIGNEE(S): University of Vermont and State Agricultural College,

USA

SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 120,433,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE: Er FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

P.	PATENT NO.			KI	IND DATE		APPLICATION NO.					ο.	DATE					
_																		
U	S 5624	919	•	Α		1997	0429		U:	S 19	94-30	0483	7	1994	0913			
M	0 9507	9507698		Al 19950323		WO 1994-US10556					56	19940914						
	W:	AM,	ΑT,	AU,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	ES,	FI,	GB,	
		GE,	HU,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LK,	LT,	LU,	LV,	MD,	MG,	MN,	MW,	
		NL,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SI,	SK,	ТJ,	TT,	UA,	UZ,	VN	
	RW:	KE,	MW,	SD,	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	
		ΝL,	PT,	SE,	BF,	BJ,	CF,	CG,								SN,	TD,	ΤG
	AU 9478374				_	19950403 AU 1994-78374												
E	EP 719144			A.	1	1996	0703		E	P 19	94-92	2924	3	1994	0914			
			-			DK,	•		-	-	-	-		-	-	PT,	SE	
JP 09504275 T2 19						1997	0428							1994				
PRIORITY APPLN. INFO.:											1204			1993				
						-		30483	-		1994							
								1	WO 1:	994-1	US10!	556		1994	0914			

OTHER SOURCE(S): MARPAT 126:350803

AB Novel trans-Pt(IV) complexes which contain heterocycle ligands such as quinoline or isoquinoline, anionic ligands such as halide or sulfate, and which optionally may contain NH3, or a primary or secondary amine are provided. The claimed compds. include, e.g., trans,trans,trans-[PtCl2(OH)2(NH3)L] (L = quinoline, isoquinoline, thiazole), mer,trans-[PtCl3(OH)(NH3)(quinoline)], trans-[PtCl4(NH3)L] (L = quinoline, isoquinoline, thiazole), trans,trans,trans-[PtCl2(O2CMe)2(NH3)(quinoline)], etc. The prepns. of these compds. are provided. These complexes have application as pharmaceuticals, in particular as antitumor agents.

IT 163921-72-0P

RL: BYP (Byproduct); PREP (Preparation)

(byproduct in prepn. of trans-Pt(IV) chloro ammine thiazole complex)

RN 163921-72-0 CAPLUS

CN Platinum, amminetrichlorohydroxy(thiazole-.kappa.N3)-, (OC-6-21)- (9CI) (CA INDEX NAME)

IT 164104-71-6P, trans-Amminedichloro(thiazole)platinum

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction with chlorine or hydrogen peroxide)

RN 164104-71-6 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

IT 163921-81-1P, trans-Amminetetrachloro(thiazole)platinum

163921-82-2P, trans, trans, trans-Amminedichlorodihydroxy(thiazole)p

latinum

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. as antitumor agent)

RN 163921-81-1 CAPLUS

CN Platinum, amminetetrachloro(thiazole-.kappa.N3)-, (OC-6-11)- (9CI) (CA INDEX NAME)

RN 163921-82-2 CAPLUS

CN Platinum, amminedichlorodihydroxy(thiazole-.kappa.N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)

applicant

ANSWER 2 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:742103 CAPLUS

DOCUMENT NUMBER: 133:304927

TITLE: Process for preparing amine platinum complexes INVENTOR(S): Wong, Ernest S. Y.; Giandomenico, Christen M.

PATENT ASSIGNEE(S): Anormed, Inc., Can. SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE _____ _____ ____ -----WO 2000-CA385 20001019 20000411 WO 2000061590 A1 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 1999-128939 P 19990413 PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 133:304927

The present invention relates to the area of Pt amine drugs. In particular, it relates to an improved process for prepq. Pt complexes PtA2LL1 (Ia) or PtA2Y2LL1 (Ib), comprising: (la) a 1st step, wherein [PtA4]2-, preferably PtCl42-, is reacted with L under appropriate conditions in a 1st solvent to form [PtA3(L)]-; (1b) a 2nd step, wherein [PtA3(L)] - is reacted with L' under appropriate conditions in a 2nd solvent to form cis-[PtA2(L')(L)]; (1c) in the case there Y is halogen or hydroxy a third step, wherein cis-[PtA2(L')(L)] is reacted with H2O2, Y2 or halogen contg. oxidant to form c,t,c-[PtA2Y2(L')(L)]; in the case where Y is carboxylate, carbamate or carbonate ester a 4th step, wherein an intermediate, where Y is hydroxy formed in step (1c), is functionalized with an appropriate acylating agent; and (1d) in the case where A is not a halide or is different from the original halide, addnl. step(s) in which the original halide A of an intermediate formed in step la or 1b, 1c or 1d is converted to a different halide or a new leaving group(s) A such as mono-dentate hydroxy, alkoxy, carboxylate or bidentate carboxylate, phosphonocarboxylate, diphosphonate, or sulfate; wherein L = amine or NH3, L' = amine but not NH3 and Y is a halogen, hydroxide, carboxylate, carbamate or carbonate ester. For example, K2[PtCl4] in N-methylpyrrolidinone reacted with 2-picoline (pic) to give K[PtCl3L]

which in aq. soln. in presence of KCl reacted with NH4OAc in presence of NH4OH to give [PtCl2(NH3)(pic)]. [PtCl2(NH3)(pic)] was oxidized by H2O2 to give to give cis,trans,cis-[PtCl2(OH)2(NH3)(pic)] which was converted to [PtCl(OH)3(NH3)(pic)] and subsequently to [PtCl(OAc)3(NH3)(pic)].

IT 301299-27-4P 301299-34-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(improved prepn. of antitumor agent)

RN 301299-27-4 CAPLUS

CN Platinum, amminedichloro(2,5-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 301299-34-3 CAPLUS

CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)

IT 301299-38-7

RL: RCT (Reactant)

(reactant for improved prepn. of platinum amine complexes as antitumor

RN 301299-38-7 CAPLUS

CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

REFERENCE(S):

6

(1) Kong; 1978, 4, CAPLUS

(2) Kong; CAN J CHEM 1978, V56(4), P441 CAPLUS

Searched by Barb O'Bryen, STIC 308-4291

(3) Rochon, F; 1988, 24, CAPLUS

(4) Rochon, F; INORG CHIM ACTA 1988, V143(1), P81 CAPLUS

(5) Talman; 1997, 14, CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

2 ANSWER 3 OF 63 CAPLUS COPYRIGHT 2001 ACS CESSION NUMBER: 2000:691638 CAPLUS

DOCUMENT NUMBER: 134:80093

TITLE: Exocyclic oxygen atoms of platinated nucleobases as

binding sites for alkali metal ions

AUTHOR(S): Freisinger, Eva; Schneider, Alexandra; Drumm, Markus;

Hegmans, Alexander; Meier, Susanne; Lippert, Bernhard

Same as N. D

CORPORATE SOURCE: Fachbereich Chemie, Universitat Dortmund, Dortmund,

D-44221, Germany

SOURCE: Dalton (2000), (19), 3281-3287

CODEN: DALTFG

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal LANGUAGE: English

Three complexes of model nucleobases with exocyclic oxygen atoms (1-methyluracilate, mura; 1-methylcytosine, mcyt; 9-methylguanine, Hmgua) which contain PtII bonded to a ring N atom and an alkali metal ion (Cs+, K+, Na+) bonded to a keto oxygen of the bases, trans-Cs[Pt(NH3) (mura)I2].cntdot.4H2O (1), trans-K[Pt(NH3)2(mcyt)2][PF6]3.cntdot.H2O (2), and trans-[Pt(NH3)(Hmgua)2(mcyt)Na(H2O)2][ClO4]3.cntdot.0.5H2O (3), were prepd. and their crystal structures detd. The compds. were studied, among others, with regard to the role of alkali metal ions for the rotation of nucleobases when bound to PtII. While in the case of 1 the alkali metal ion is necessary for charge compensation and for this reason its binding to the platinated mura is not fully unexpected, it is surprising to see that alkali metal ions even bind to cationic complexes of PtII contg. neutral nucleobases (2, 3).

IT 315662-46-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure)

RN 315662-46-5 CAPLUS

CN Cesium(1+), diaqua-, (SP-4-1)-amminediiodo(1-methyl-2,4(1H,3H)-pyrimidinedionato-.kappa.N3)platinate(1-), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 315662-45-4

CMF C5 H8 I2 N3 O2 Pt . Cs H4 O2

CM 2

CRN 315662-44-3

CMF C5 H8 I2 N3 O2 Pt

CCI CCS

CDES 7:SP-4-1

CM 3

CRN 81009-40-7 CMF Cs H4 O2 CCI CCS

H₂O-Cs⁺OH₂

IT 315662-52-3P

RN 315662-52-3 CAPLUS

CN Platinum(2+), tetraammine-, (SP-4-1)-, bis[(SP-4-1)-amminediiodo(1-methyl-2,4(1H,3H)-pyrimidinedionato-.kappa.N3)platinate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 315662-44-3 CMF C5 H8 I2 N3 O2 Pt CCI CCS CDES 7:SP-4-1

CM 2

CRN 16455-68-8 CMF H12 N4 Pt CCI CCS CDES 7:SP-4-1

161269-39-2 IT

RL: RCT (Reactant)

(reactant for prepn. of sodium platinum ammine methylcytosine methylguanine complex)

161269-39-2 CAPLUS RN

Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)amminediiodo-, CN (SP-4-1)-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

REFERENCE(S):

53

(1) Addison, A; J Chem Soc, Dalton Trans 1984, P1349 CAPLUS

(2) Bax, A; J Magn Reson 1985, V63, P207 CAPLUS

(3) Chaput, J; Proc Natl Acad Sci USA 1999, V96, P10614 CAPLUS

(4) Cheong, C; Biochemistry 1992, V31, P8406 CAPLUS

(5) Coste, F; Nucl Acids Res 1999, V27, P1837 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2001 ACS ANSWER 4 OF 63

CCESSION NUMBER: DOCUMENT NUMBER:

2000:494736 CAPLUS

TITLE:

133:217276 Steric control of DNA interstrand cross-link sites of trans platinum complexes: specificity can be dictated

by planar nonleaving groups

AUTHOR(S):

Brabec, Viktor; Neplechova, Kamila; Kasparkova, Jana;

Farrell, Nicholas

CORPORATE SOURCE:

Academy of Sciences of the Czech Republic, Brno,

61265, Czech Rep.

SOURCE:

JBIC, J. Biol. Inorg. Chem. (2000), 5(3), 364-368

CODEN: JJBCFA; ISSN: 0949-8257

PUBLISHER:

Springer-Verlag

DOCUMENT TYPE:

Journal

LANGUAGE:

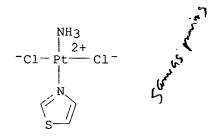
English

Recent findings that novel trans-dichloroplatinum(II) complexes exhibit antitumor activity violate the classical structure-activity relationships of platinum(II) complexes. These novel "nonclassical" trans platinum complexes also comprise those contq. planar arom. amines. Initial studies have shown that these compds. form a considerable amt. of DNA interstrand cross-links (up to .apprx.30%) with a rate markedly higher than clin. ineffective transplatin. The present work has shown, using Maxam-Gilbert footprinting, that trans-[PtCl2(NH3)(quinoline)] and trans[PtCl2(NH3)(thiazole)], representatives of the group of new antitumor trans-dichloroplatinum complexes contg. planar amines, preferentially form DNA interstrand cross-links between guanine residues at the 5'-GC-3' sites. Thus, DNA interstrand crosslinking by trans-[PtCl2(NH3)(quinoline)] and trans-[PtCl2(NH3)(thiazole)] is formally equiv. to that by antitumor cisplatin, but different from clin. ineffective transplatin which preferentially forms these adducts between complementary guanine and cytosine residues. This result shows for the first time that simple chem. modification of the structure of an inactive compd. alters its DNA binding site into a DNA adduct of an active drug. 164104-71-6

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (steric control of DNA interstrand cross-link sites of trans platinum complexes)

RN 164104-71-6 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: REFERENCE(S):

3

(1) Farrell, N; J Med Chem 1989, V32, P2240 CAPLUS

(2) Farrell, N; Transition metal complexes as drugs and chemotherapeutic agents, chaps 2 and 3 1989

(3) van Beusichem, M; Inorg Chem 1992, V31, P634 CAPLUS

LZ ANSWER 5 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACÇESSION NUMBER:

2000:494729 CAPLUS

DOCUMENT NUMBER:

133:217275

TITLE:

ΙT

Kinetics and mechanism for reduction of

anticancer-active tetrachloroam(m)ine platinum(IV)

compounds by glutathione

AUTHOR(S):

Lemma, Kelemu; Berglund, Johan; Farrell, Nicholas;

Elding, Lars I.

CORPORATE SOURCE:

Inorganic Chemistry 1, Chemical Center, Lund

University, Lund, SE-22100, Swed.

SOURCE:

JBIC, J. Biol. Inorg. Chem. (2000), 5(3), 300-306

CODEN: JJBCFA; ISSN: 0949-8257

PUBLISHER:

Springer-Verlag

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Glutathione (GSH) redn. of the anti-cancer-active platinum(IV) compds. trans-[PtCl4(NH3)(thiazole)] (1), trans-[PtCl4(cha)(NH3)] (2), cis-[PtCl4(cha)(NH3)] (3) (cha = cyclohexylamine), and cis-[PtCl4(NH3)2] (4) has been investigated at 25.degree.C in a 1.0 M aq. medium at pH 2.0-5.0 (1) and 4.5-6.8 (2-4) using stopped-flow spectrophotometry. The redox reactions follow the second-order rate law d[Pt(IV)]/dt=k[GSH]tot[Pt(IV)], where k is a pH-dependent rate const. and [GSH]tot the total concn. of glutathione. The redn. takes place via parallel reactions between the platinum(IV) complexes and the various

protolytic species of glutathione. The pH dependence of the redox kinetics is ascribed to displacement of these protolytic equil. thiolate species GS- is the major reductant under the reaction conditions used. The second-order rate consts. for redn. of compds. 1-4 by GS- are (1.43.+-.0.01) .times. 107, (3.86.+-.0.03) .times. 106, (1.83.+-.0.01).times. 106, and (1.18.+-.0.01) .times. 106 M-1 s-1, resp. Rate consts. for redn. of 1 by the protonated species GSH are more than five orders of magnitude smaller. The mechanism for the reductive elimination reactions of the Pt(IV) compds. is proposed to involve an attack by glutathione on one of the mutually trans coordinated chloride ligands, leading to two-electron transfer via a chloride-bridged activated complex. kinetics results together with literature data indicate that platinum(IV) complexes with a trans Cl-Pt-Cl axis are reduced rapidly by glutathione as well as by ascorbate. In agreement with this observation, cytotoxicity profiles for such complexes are very similar to those for the corresponding platinum(II) product complexes. The rapid redn. within 1 s of the platinum(IV) compds. with a trans Cl-Pt-Cl axis to their platinum(II) analogs does not seem to support the strategy of using kinetic inertness as a parameter to increase anticancer activity, at least for this class of compds.

163921-81-1

IT

RN

CN

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(redn. kinetics of anticancer-active tetrachloroam(m)ine platinum(IV)
compds. by glutathione)

163921-81-1 CAPLUS

Platinum, amminetetrachloro(thiazole-.kappa.N3)-, (OC-6-11)- (9CI) (CA INDEX NAME)

REFERENCE COUNT: REFERENCE(S):

58

- (1) Allison, W; Acc Chem Res 1976, V9, P293 CAPLUS
- (2) Appleton, T; Inorg Chem 1989, V28, P2030 CAPLUS
- (3) Bancroft, D; J Am Chem Soc 1990, V112, P6860 CAPLUS
- (4) Barnard, C; Topics in biological inorganic chemistry 1999, V1, P45 CAPLUS
- (5) Berglund, J; Inorg Chem 1994, V33, P3346 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 63 ACCESSION NUMBER: DOCUMENT NUMBER: TITLE:

CAPLUS COPYRIGHT 2001 ACS 1999:411016 CAPLUS

131:152998

Synthesis, Structure, Biological Activity, and DNA Binding of Platinum(II) Complexes of the Type trans-[PtCl2(NH3)L] (L = Planar Nitrogen Base). Effect of L and Cis/Trans Isomerism on Sequence Specificity

and Unwinding Properties Observed in Globally Platinated DNA

Bierbach, Ulrich; Qu, Yun; Hambley, Trevor W.; AUTHOR(S):

Peroutka, John; Nguyen, Holly L.; Doedee, Marijo;

Farrell, Nicholas

CORPORATE SOURCE: Department of Chemistry, Virginia Commonwealth

University, Richmond, VA, 23284-2006, USA

Inorg. Chem. (1999), 38(15), 3535-3542

CODEN: INOCAJ; ISSN: 0020-1669

American Chemical Society

PUBLISHER: DOCUMENT TYPE:

SOURCE:

Journal

LANGUAGE:

English AB

To establish fundamental structural requirements for the antitumor activation of the trans-platinum geometry, complexes [PtCl2(NH3)L] (L = planar N donor) were synthesized. The trans isomers, trans-[PtCl2(NH3)(quinoline)] (3), trans-[PtCl2(NH3)(thiazole)] (5), trans-[PtCl2(NH3)(benzothiazole)] (7), and trans-[PtCl2(NH3)(isoquinoline)] (8) and the cis isomers cis-[PtCl2(NH3)(quinoline)] (4) and cis-[PtCl2(NH3)(thiazole)] (6) were characterized by 1H NMR and anal. data. The crystal structures of 3, 5, 7, and 8 were detd.: 3, monoclinic, space group P21/c, with a 8.414(1), b 12.373(3), c 21.266(3) .ANG., .beta. 96.78(1).degree. and Z = 8; 5, monoclinic, space group P21/n, with a 8.815(4), b 19.917(8), c 14.498(5) .ANG., .beta. 103.30(3).degree. and Z = 12; 7, monoclinic, P21/c, with a 8.150(4), b 23.196(9), c 11.297(7) .ANG., .beta. 90.94(4).degree. and Z = 8; 8, monoclinic, C2/c, with a 19.043(4), b 8.570(2), c 29.127(6) .ANG., .beta. 111.59(2).degree. and Z = 16. In all cases, the Pt coordination plane and L are mutually twisted with angles between planes of 50-68.degree.. Bulky quinoline in 3 produces intramol. steric strain as evidenced by a short, nonbonding Pt.cntdot..cntdot..cntdot.H8quin contact of 2.77 .ANG. and concomitantly distorted Pt-Nquin-C bond angles. The trans complexes 3, 5, 7, and 8 showed a significantly higher cytotoxicity in cisplatin-sensitive L1210 leukemia than trans-[PtCl2(NH3)2] (2), with 3 and 5 being as potent as the corresponding cis isomers 4 and 6. presence of the planar ligand greatly enhanced the activity of all of the compds. in cells resistant to cisplatin, cis-[PtCl2(NH3)2] (1). geometry and L play an important role in the binding of 1-7 to DNA. For synthetic poly(dG).cntdot.poly(dC) and poly(dG-dC).cntdot.poly(dG-dC) theorder of binding affinities (rb, drug-to-nucleotide ratio) was 2 > 1 > 6 >5 > 4 > 7 > 3 and 5 > 6 > 7 > 3 > 2 > 1 > 4, resp. also, 3 and 7, carrying large planar ligands, were remarkably effective at unwinding neg. supercoiled, closed circular pUC19 DNA (.phi. = 15.degree. and 17.degree., resp.). The consequences of structural effects caused by L on target DNA with respect to possible biol. consequences are discussed.

IT 114502-44-2P, cis-Amminedichloro(thiazole)platinum RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn., antitumor activity and DNA binding)

RN 114502-44-2 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

IT 164104-71-6P, trans-Amminedichloro(thiazole)platinum

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)

(prepn., crystal structure, antitumor activity and DNA binding)

RN 164104-71-6 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

REFERENCE(S): (1) Abrams, M; Inorg Chim Acta 1987, V131, P3 CAPLUS

(2) Abrams, M; Science 1993, V261, P725 CAPLUS

(3) Albinati, A; Inorg Chem 1990, V29, P1812 CAPLUS

(5) Barnham, K; J Chem Soc Chem Commun 1994, P721

CAPLUS

(7) Bellon, S; Biochemistry 1991, V30, P8026 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 7 OF 63 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1999:346517 CAPLUS

DOCUMENT NUMBER: 131:110357

TITLE: A Major, pH-Induced Stereochemical Switch of Pairs of

trans-Oriented Ligands in Complexes of trans-a2PtII (a

= NH3, CH3NH2)

AUTHOR(S): Mueller, Jens; Glahe, Frank; Freisinger, Eva; Lippert,

Bernhard

CORPORATE SOURCE: Fachbereich Chemie, Universitaet Dortmund, Dortmund,

D-44221, Germany

SOURCE: Inorg. Chem. (1999), 38(13), 3160-3166

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Trans-[Pt(CH3NH2)2(1-MeC-N4)2]X2 (3a, X = NO3-; 3b, X = ClO4-), contg. the model nucleobase 1-methylcytosine (1-MeC) platinated at N4 and protonated at N3, hence in its rare tautomeric form, was prepd. from the PtIV

precursor trans, trans-[Pt(CH3NH2)2(1-MeC-

N4)2(OH)2](NO3)2.cntdot.2H2O (2) upon redn. with H2. Crystn. of 3a from 1 M NaOH afforded trans-[Pt(CH3NH2)2(1-MeC--N4)2].cntdot.4H2O (4a) or,

following lyophilization and deprotonation in CH3OH by Me3CONa, gave trans-[Pt(CH3NH2)2(1-MeC--N4)2].cntdot.2CH3OH (4b). While dihedral angles between the coplanar bases and the PtN4 planes are large in the case of 2 (84.8(1).degree.) and 3b (73.9(1).degree.), they become markedly smaller in 4a (55.5(2).degree.) and 4b (26.6(2).degree.) as a consequence of pairwise intramol. H bonding between the NH protons of the CH3NH2 groups and the N3 positions of the cytosine nucleobases. DFT calcns. for the corresponding NH3 complex gave a dihedral angle of 22.3 degree. switch of the mutually trans-oriented ligand pairs from approx. perpendicular to roughly coplanar appears to take place during the crystn. process, probably because of competition between intramol. H bonding and intermol. H bonding with the solvent. Crystal data: 2, triclinic, space group P.hivin.1, a 5.937(1), b 8.228(2), c 12.470(2) .ANG., .alpha. 80.36(3), .beta. 80.80(3), .gamma. 80.54(3).degree., Z = 2; 3b, triclinic, P.hivin.1, a 7.392(1), b 9.072(2), c 10.047(2) .ANG., .alpha. 112.40(3), .beta. 106.07(3), .gamma. 94.66(3).degree., Z = 2; 4a, triclinic, P.hivin.1, a 7.104(1), b 7.549(2), c 9.209(2) .ANG., .alpha. 87.74(3), .beta. 88.04(3), .gamma. 85.92(3).degree., Z = 2; 4b, triclinic, P.hivin.1, a 7.045(1), b 7.421(1), c 9.966(2) .ANG., .alpha. 109.25(3), .beta. 99.22(3), .gamma. 95.02(3).degree., Z = 2.

IT 230622-36-3P

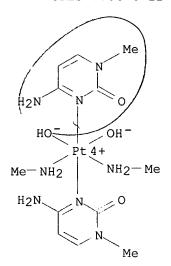
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and isomerization in study of pH induced stereochem. switch)

RN 230622-36-3 CAPLUS CN Platinum(2+), bis(4

Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)dihydroxybis(methanamine)-, (OC-6-12)-, dinitrate (9CI) (CAINDEX NAME)

CM 1

CRN 230622-35-2 CMF C12 H26 N8 O4 Pt CCI CCS CDES 7:OC-6-12



CM 2

CRN 14797-55-8 CMF N O3

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0 = N - 0 -
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REFERENCE COUNT:

REFERENCE(S):

(1) Arpalahti, J; Inorg Chem 1990, V29, P2564 CAPLUS

(2) Ashton, P; J Am Chem Soc 1998, V120, P11932 CAPLUS

(3) Biagini-Cingi, M; Inorg Chim Acta 1984, V86, P137 CAPLUS

(4) Bissell, R; Nature 1994, V369, P133 CAPLUS

(5) Blake, A; J Chem Soc Dalton Trans 1998, P2597

CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 8 OF 63 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1998:223265 CAPLUS

DOCUMENT NUMBER:

128:303325

TITLE:

Metal-Stabilized rare tautomers of nucleobases. Part

7. Affinity of the iminooxo tautomer anion of

1-methylcytosine in trans-[Pt(NH3)2(1-MeC-N4)2]2+ for

heterometals

AUTHOR(S):

SOURCE:

Muller, Jens; Zangrando, Ennio; Pahlke, Norbert; Freisinger, Eva; Randaccio, Lucio; Lippert, Bernhard Fachbereich Chemie, Universitat Dortmund, Dortmund,

CORPORATE SOURCE:

D-44221, Germany

Chem. -- Eur. J. (1998), 4(3), 397-405 CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: LANGUAGE:

Journal English

Reaction of a PtII complex contg. two 1-methylcytosine (1-MeC) nucleobases bound through the exocyclic amino group N4, trans-[Pt(NH3)2(1-MeC-N4)2](NO3)2 (1), with the heterometal species [(dien)Pd]2+ or Hg2+ gives trans-[(NH3)2Pt[(N4-1-MeC--N3)Pd(dien)]2](ClO4)4.cntdot.2H2O(3) and trans-[(NH3)2Pt(N4-1-MeC--N3)2Hg](NO3)2.cntdot.2H2O (4), resp. The heterometals are bound through the N3 positions of the two cytosine rings. 1 Contains the nucleobase as its rare iminooxo tautomer. In the solid-state structure of 1, the two nucleobases display a syn orientation between Pt and the endocyclic N3 position, whereas in 3 they adopt an anti conformation. In both compds. the cytosine bases are in a head-to-tail orientation. In the bimetallic 4 however, the 1-methylcytosine ligands are head-to-head and syn with the two nucleobases acting as chelating ligands. The Pt-Hg distance in 4 is guite short (2.7498(6) .ANG.), suggesting a weak bonding interaction. In 3 the Pt-Pd distance (5.13 .ANG.) is too long for any interaction. While H-bond formation between the iminooxo tautomer of 1-MeC in 1 with free 1-MeC and likewise between the deprotonated form trans-[Pt(NH3)2(1-MeC--N4)2] (2) and free 9-ethylguanine (9-EtGH) is possible only if the cytosine bases are in an anti orientation, there is no indication for such H-bonding patterns from 1H NMR studies.

TT 101152-06-1

RN

RL: RCT (Reactant)

(prepn. of)

101152-06-1 CAPLUS

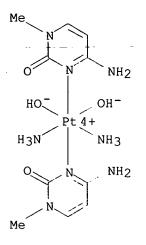
CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-

.kappa.N3)diamminedihydroxy-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

CRN 101152-05-0

CMF C10 H22 N8 O4 Pt CCI CCS CDES 7:0C-6-12



2 CM

CRN 14797-55-8 CMF и оз

- o -- N-

L22 ANSWER 9 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1998:1819 CAPLUS

DOCUMENT NUMBER:

128:94638

TITLE:

Analysis of vicinal optical activity of platinum(II)

complexes containing trans-[PtN202] chromophore

AUTHOR(S):

Klyagina, A. P.; Golovaneva, I. F.; Burkov, V. I.;

Minacheva, L. Kh.; Sadikov, G. G.

CORPORATE SOURCE:

Inst. Obshch. Neorg. Khim. im. Kurnakova, Moscow,

Russia

SOURCE:

Zh. Neorg. Khim. (1997), 42(6), 966-968

CODEN: ZNOKAQ; ISSN: 0044-457X

PUBLISHER: DOCUMENT TYPE: MAIK Nauka Journal

LANGUAGE:

Russian

AB Electronic transition responsible for absorption spectra and CD of platinum complexes with proline and hydroxyproline ligands were analyzed. The CD was interpreted in terms of the one-electron model of the optical activity. The pos. value of the pseudo-scalar function corresponding to the chromophore symmetry correlated with the pos. Cotton effect in a region of the dipole-splitted transition and to the neg. Cotton effect connected with the magneto-splitted transition.

38991-52-5 IT

RL: PRP (Properties)

(anal. of vicinal optical activity of platinum(II) complexes contg. trans-[PtN2O2] chromophore)

RN 38991-52-5 CAPLUS

H+

L22 ANSWER 10 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:295135 CAPLUS

DOCUMENT NUMBER: 126:311303

JOCOMENI NOMBER. 120.511505

TITLE: Platinum(II) nucleobase complexes containing up to four different ligands: syntheses and x-ray structure

determinations of cis-[PtI(1-MeC)2(NH3)]ClO4 and

[PtI(1-MeC)(9-EtGH)(NH3)]ClO4.cntdot.1.5H2O

AUTHOR(S): Wienkotter, Thomas; Sabat, Michal; Trotscher-Kaus,

Gabriele; Lippert, Bernhard

CORPORATE SOURCE: Fachbereich Chemie, Univ. Dortmund, Dortmund, D-44221,

Germany

SOURCE: Inorg. Chim. Acta (1997), 255(2), 361-366

CODEN: ICHAA3; ISSN: 0020-1693

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

A square-planar Pt(II) complex contg. four different ligands, including the two model nucleobases 1-methylcytosine (1-MeC) and 9-ethylguanine (9-EtGH), was prepd. and studied by x-ray crystallog. [PtI(1-MeC)(9-EtGH)(NH3)]ClO4.cntdot.1.5H2O(1) crystallizes in the monoclinic system, space group C2/c with a 16.577(3), b 16.638(2), c 17.923(3) .ANG., .beta. 114.37(1).degree., Z = 8. The two nucleobases which are platinated at N3 (1-MeC) and N7 (9-EtGH) are cis to each other and oriented in a way as to form a very weak H bond (3.39 .ANG.) between NH2(4) of 1-MeC and O(6) of 9-EtGH. The guanine ligand is trans to I-. The title compd. represents one of three possible geometrical isomers of compds. having this compn. A closely related complex, cis-[PtI(1-MeC)2(NH3)]Cl04 (3), has likewise been isolated and x-ray structurally characterized: triclinic system, space group P.hivin.1 with a 10.490(4), b 10.886(4), c 9.529(3) .ANG., .alpha. 94.18(3), .beta. 106.28(3), .gamma. 106.33(3).degree., Z = 2. In 3 the two 1-MeC bases are platinated at N3 and oriented head-tail, with intramol. H bonds of 3.22 and 2.95 .ANG. between pairs of NH2(4) and O(2) groups.

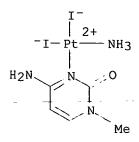
IT 161269-39-2

RL: RCT (Reactant)

(for prepn. of platinum(II) nucleobase complexes contg. up to four different ligands)

RN 161269-39-2 CAPLUS

CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)amminediiodo-, (SP-4-1)- (9CI) (CA INDEX NAME)



122 ANSWER 11 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1997:294759 CAPLUS

DOCUMENT NUMBER:

126:311299

TITLE:

H3O2- bridging in a Pt(IV) nucleobase complex leading

to infinite chains: trans, trans, trans-[Pt(NH3)2(1-

MeU) 2 (H3O2)] n (NO3) n. cntdot. (4H2O) n (1-MeU =

1-methyluracilate)

AUTHOR(S):

Lianza, Francesca; Albinati, Alberto; Lippert,

Bernhard

CORPORATE SOURCE:

Ist. Chimico Farmaceutico, Univ. Milano, Milan,

I-20131, Italy

SOURCE:

Inorg. Chim. Acta (1997), 255(2), 313-318

CODEN: ICHAA3; ISSN: 0020-1693

PUBLISHER: DOCUMENT TYPE:

Elsevier Journal

LANGUAGE:

Journal English

The prepn. and x-ray crystal structure detn. of a Pt(IV) nucleobase complex, trans, trans, trans-[Pt(NH3)2(1-MeU)2(H3O2)]n(NO3)n.cntdot.(4H2O)n (1-MeU = 1-methyluracilate-N3) is reported. The compd., obtained upon recrystn. of trans, trans, trans-[Pt(NH3)2(1-MeUH)2(OH)2](NO3)2 (1-MeUH = neutral 1-methyluracil-N3) from water, crystallizes in the triclinic system, space group P.hivin.1 with two independent cations in the unit cell: a 7.3023(8), b 10.1470(20), c 13.4220(20) .ANG., .alpha. 78.800(17), .beta. 83.580(9), .gamma. 78.930(10).degree., Z = 2. Description of its solid state structure as a H3O2- compd. rather than a genuine mixed H2O,OH- complex is based on the presence of very short H bonds of 2.450(6) .ANG. between the oxygens of axial aqua and hydroxo ligands of adjacent Pt(IV) cations, leading to infinite chains.

IT 129700-79-4

RL: RCT (Reactant)

(for prepn. of platinum methyluracilato ammine hydroxo aqua infinite chain complex)

RN 129700-79-4 CAPLUS

CN Platinum(2+), diamminedihydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedione-.kappa.N3)-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

CRN 129700-78-3

CMF C10 H20 N6 O6 Pt

CCI CCS

CDES 7:OC-6-12

CM 2

CRN 14797-55-8 CMF N O3

0

0= N-0-

IT 189180-10-7P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure and hydrogen bonding)

RN 189180-10-7 CAPLUS

CN Platinum(1+), diammineaquahydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedionato-.kappa.N3)-, (OC-6-23)-, nitrate, tetrahydrate (9CI) (CA INDEX NAME)

CM 1

CRN 189180-09-4

CMF C10 H19 N6 O6 Pt . N O3

CM 2

CRN 189180-08-3

CMF C10 H19 N6 O6 Pt

CCI CCS

CDES 7:OC-6-23

CM 3

CRN 14797-55-8 CMF N 03

L22 ANSWER 12 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1996:492707 CAPLUS

DOCUMENT NUMBER:

125:185094

TITLE:

Immunocytochemical labeling of aerobic and hypoxic

mammalian cells using a platinated derivative of EF5 Matthews, J.; Adomat, H.; Farrell, N.; King, P.; Koch,

C.; Lord, E.; Palcic, B.; Poulin, N.; Sangulin, J.;

Skov, K.

CORPORATE SOURCE:

Department Medical Biophysics, BC Cancer Research

Centre, Vancouver, BC, V5Z 1L3, Can.

SOURCE:

Br. J. Cancer, Suppl. (1996), 74(27), S200-S203

CODEN: BJCSB5; ISSN: 0306-9443

DOCUMENT TYPE:

Journal

LANGUAGE:

AUTHOR(S):

English

AB The monoclonal antibody ELK3-51 was previously developed to detect adducts of the 2-nitroimidazole EF5. Direct immunofluorescence was used to detect adducts of EF5 or of a platinated deriv. cis-[PtCl2(NH3)EF5] in SCCVII cells treated under aerobic or hypoxic conditions. Fluorescence measurements of these cells using both image and flow cytometric methods were compared, giving similar profiles. Platination significantly decreased immunofluorescence levels (.apprx.4-fold less than EF5) after 3 h in hypoxia, but also increased levels after exposure in air (.apprx.1.5 .times.) such that the hypoxic ratio decreased from .apprx.50 to .apprx.13. Platinated EF5 also showed significantly greater cytotoxicity than its parent in both aerobic and hypoxic cells. These results are consistent with targeting of EF5 to DNA, which was confirmed qual. by confocal microscopy.

IT180990-37-8

RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (immunocytochem. labeling of aerobic and hypoxic mammalian cells using a platinated deriv. of EF5)
180990-37-8 CAPLUS
Platinum, amminedichloro[2-nitro-N-(2,2,3,3,3-pentafluoropropyl)-1Himidazole-1-acetamide-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN

CN

L22 ANSWER 13 OF 63 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1996:490063 CAPLUS

DOCUMENT NUMBER: 125:211928

TITLE: New perfluorophthalate complexes of platinum(II) with

chemotherapeutic potential

AUTHOR(S): de Oliveira, M. B.; Miller, J.; Banks, R. E.; Kelland,

L. R.; McAuliffe, C. A.; Mahmood, N.; Rowland, J. J.

CORPORATE SOURCE: Dep. Chem., Fed. Univ. Paraiba, Joao Pessoa,

58059-000, Brazil

SOURCE: Met.-Based Drugs (1996), 3(3), 117-122

CODEN: MBADEI; ISSN: 0793-0291

DOCUMENT TYPE: Journal LANGUAGE: English

AB Two new platinum(II) complexes have been synthesized and their anti-tumor and anti-HIV activities have been evaluated. The new complexes are: (i) cis-tetrafluorophthalate-ammine-morpholine-platinum(II) or MMF3 and (ii) cis-tetrafluorophthalate-ammine-piperidine-platinum(II) or MPF4. They were characterized by elemental anal., IR spectra and 1H and 13C NMR spectra. They were tested against five human ovarian carcinoma cell lines, viz., CH1, CH1cisR, A2780, A2780cisR and SKOV-3. They were less active than cis-platin and showed cross-resistance with cis-platin in the CH1cisR and A2780cisR acquired resistance lines. They were also tested for possible anti-HIV activity using the HIV-I IIIB virus and C8166 cells, but they were inactive compared with AZT.

IT 181276-56-2P 181276-57-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antitumor and anti-HIV activities of new perfluorophthalate complexes with platinum(II) in human cells)

RN 181276-56-2 CAPLUS

CN Platinum, ammine(morpholine-N4)[3,4,5,6-tetrafluoro-1,2-benzenedicarboxylato(2-)-O1,O2]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 181276-57-3 CAPLUS

CN Platinum, ammine(piperidine)[3,4,5,6-tetrafluoro-1,2-benzenedicarboxylato(2-)-01,02]-, (SP-4-3)- (9CI) (CA INDEX NAME)

$$N - R$$

IT 103436-53-9P 116235-97-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (antitumor and anti-HIV activities of new perfluorophthalate complexes with platinum(II) in human cells)

RN 103436-53-9 CAPLUS

CN Platinum, amminediiodo(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-97-3 CAPLUS

CN Platinum, amminediiodo(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

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2+
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ANSWER 14 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:621706 CAPLUS

DOCUMENT NUMBER: 123:46735

TITLE: Trans platinum(IV) complexes

INVENTOR(S): Farrell, Nicholas

PATENT ASSIGNEE(S): University of Vermont and State Agricultural College,

USA

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                     KIND
                           DATE
                                          APPLICATION NO.
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                                                           _____
    WO 9507698
                      Α1
                           19950323
                                          WO 1994-US10556
                                                          19940914
            AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,
            GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,
            NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN
        RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,
            NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
    US 5624919
                      Α
                           19970429
                                          US 1994-304837
                                                           19940913
    AU 9478374
                      A1
                           19950403
                                          AU 1994-78374
                                                           19940914
    EP 719144
                      A1
                           19960703
                                          EP 1994-929243
                                                           19940914
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
                    · T2
                           19970428
                                          JP 1994-509398
                                                           19940914
    JP 09504275
PRIORITY APPLN. INFO.:
                                       US 1993-120433
                                                           19930914
                                       US 1994-304837
                                                           19940913
                                       WO 1994-US10556
                                                           19940914
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OTHER SOURCE(S): MARPAT 123:46735

Novel trans(platinum)(IV) complexes contg. planar heteroarom. ligands are presented as well as methods for their prepn. These complexes are to be used as pharmaceutical agents, e.g., for the treatment of cancer and parasitic diseases.

TΤ 163921-72-0P

RL: BYP (Byproduct); PREP (Preparation)

(prepn. of trans platinum(IV) nitrogen heterocycle complexes)

RN 163921-72-0 CAPLUS

CN Platinum, amminetrichlorohydroxy(thiazole-.kappa.N3)-, (OC-6-21)- (9CI) (CA INDEX NAME)

Cl- Cl- Cl- Cl- N S

INDEX NAME)

RN 163921-82-2 CAPLUS
CN Platinum, amminedichlorodihydroxy(thiazole-.kappa.N3)-, (OC-6-12)- (9CI)
(CA INDEX NAME)

H₃N Cl-

RN 164104-71-6 CAPLUS
CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

AΒ

L22 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:699368 CAPLUS

DOCUMENT NUMBER: __ 123:132005

TITLE: W) Synthesis and in Vitro and in Vivo Antitumor Activity

of a Series of Trans Platinum Antitumor Complexes AUTHOR(S): Kelland, Lloyd R.; Barnard, F. J.; Evans, Iona G.;

Murrer, Barry A.; Theobald, Brian R. C.; Wyer, Sandra

B.; Goddard, Phyllis M.; Jones, Mervyn; Valenti,

Malania, at al

Melanie; et al.

CORPORATE SOURCE: CRC Centre for Cancer Therapeutics, Institute of

Cancer Research, Sutton/Surrey, SM2 5NG, UK

SOURCE: J. Med. Chem. (1995), 38(16), 3016-24

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal LANGUAGE: English

The synthesis of a series of platinum complexes of trans coordination geometry [centered around the general formula, transammine(amine)dichlorodihydroxoplatinum(IV) plus corresponding tetrachloroplatinum(IV) or Pt(II) counterparts] is described as part of a drug discovery program to identify more effective platinum-based anticancer drugs, particularly targeted toward the circumvention of resistance to cisplatin. Complexes have been evaluated for antitumor activity using in vitro and in vivo tumor models. In vitro against a panel of cisplatin-sensitive and -resistant human tumor cell lines (predominantly ovarian), many of the trans platinum complexes studied (e.g., cyclohexyl) exhibited comparable potency to cisplatin and also overcame acquired cisplatin resistance, where resistance was due mainly to either reduced drug uptake or enhanced platinum-DNA adduct removal. Morever, 14 trans complexes showed significant in vivo antitumor activity against the s.c. murine ADJ/PC6 plasmacytoma model; all were platinum(IV) complexes, 13/14 possessing axial hydroxo ligands the other possessing axial ethylcarbamato ligands. Where tested, all of their resp. platinum(II) or tetrachloroplatinum(IV) counterparts were inactive. Notably, three dihydroxoPt(IV) complexes (c-hexyl, c-heptyl, and 1-adamantyl) retained some efficacy against a cisplatin-resistant variant of the ADJ/PC6. Compds. $\{trans-[PtCl2(OH)2NH3(RNH2)]\}$ R = c-C6H11, 22, R = Me3C, 27, R = n-C6H13, 28, R = PhCH2, and {trans-[PtBr2(OH)2NH3(c-C6H11NH2)]} also produced evidence of antitumor activity (>5 days growth delay) against s.c. grown advanced stage human ovarian carcinoma xenografts. These data demonstrate that a series of transammine(amine)dichlorodihydroxoplatinum(IV) complexes are active in vivo against both murine and human s.c. tumor models and represent potential leads to a new generation of platinum-based anticancer drug.

IT 166403-99-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and antitumor activity of trans platinum antitumor

complexes)

RN 166403-99-2 CAPLUS

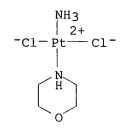
CN Platinum, amminedichlorodihydroxy(piperidine)-, (OC-6-12)- (9CI) (CA INDEX NAME)

IT 166583-70-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (synthesis and antitumor activity of trans platinum antitumor complexes)

RN 166583-70-6 CAPLUS

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-1)- (9CI) (CA INDEX NAME)



ANSWER 16 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1995:380922 CAPLUS

DOCUMENT NUMBER:

122:150172

TITLE:

Dimerization of trans-[Pt(NH3)(1-MeC-N3)(H2O)2]2+ and Oxidation to a Diplatinum(III) Species in the Presence

of Glycine. Relevance for Platinum Cytosine Blue Wienkoetter, Thomas; Sabat, Michal; Fusch, Gerd;

Lippert, Bernhard

CORPORATE SOURCE:

Fachbereich Chemie, Universitaet Dortmund, Dortmund,

D-44221, Germany

SOURCE:

Inorg. Chem. (1995), 34(5), 1022-9

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE:

Journal

LANGUAGE:

AUTHOR(S):

English

Trans-Pt(NH3)(1-MeC=N3)I2 (4) with 1-MeC (1-methylcytosine) bound to Pt Via N(3), obtained from cis-[Pt(NH3)2(1-MeC-N3)C1]C1, gives trans-[Pt(NH3)(1-MeC-N3)(H2O)2]2+ when treated with 2 equiv of-AgNO3. This diaqua species rapidly dimerizes in soln. to give [Pt2(NH3)2(1-MeC--N3,N4)2(H2O)2]2+ (5), a compd. contg. bridging 1-methylcytosinato ligands in a head-tail arrangement, as judged from 1H NMR spectroscopy. Also an intensely purple, paramagnetic species 5' forms, which is yet another representative of the class of Pt pyrimidine blues. If dimerization to give 5 is carried out in the presence of the amino acid glycine, spontaneous oxidn. to a yellow diplatinum(III) complex [Pt2(NH3)2(1-MeC--N3,N4)2(gly-N,O)2](NO3)2.cntdot.3H2O (6) takes place. The compd. was isolated and characterized by NMR spectroscopy (1H, 195Pt) and x-ray crystallog.: triclinic system, space group P.hivin.1, a

12.438(4), b 12.820(4), c 10.275(2) .ANG., .alpha. 98.21(3), .beta. 112.84(2), .gamma. 62.24(2).degree., Z = 2. In 6, the two methylcytosinato rings are oriented head-tail, and glycinate anions chelate Pt atoms via NH2 (axial) and COO- (equatorial). The Pt-Pt bond length is 2.527(1) .ANG.. When L-alanine is applied instead of glycine, a complex analogous to 6 is formed which occurs in soln. in two diastereomeric forms, however, as evident from 1H NMR spectroscopy. 5, an oligomerization process leading to Pt cytosine blue is proposed, according to which O(2) of 1-MeC- is involved in bridging dinuclear entities or dinuclear and mononuclear entities. The proposed oligomerization principle differs markedly from that obsd. in tetranuclear (Pt2.25+)4 complexes contg. cyclic amidate ligands.

IT 161269-39-2P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and aquation using silver nitrate)

RN 161269-39-2 CAPLUS

Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)amminediiodo-, CN (SP-4-1)-(9CI) (CA INDEX NAME)

L22 ANSWER 17 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:104236 CAPLUS

DOCUMENT NUMBER: 124:248674

TITLE: The synthesis and characterization of dinuclear

platinum complexes bridged by the 4,4'-

dipyrazolylmethane ligand

Broomhead, John A.; Lynch, Mark J. AUTHOR(S):

CORPORATE SOURCE: Department of Chemistry, Australian National

University, Canberra, ACT, 0200, Australia Inorg. Chim. Acta (1995), 240(1-2), 13-17

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal LANGUAGE: English

Monobridged-dinuclear Pt(II) complexes, where the bridging ligand is 4,4'-dipyrazolylmethane (dpzm), were prepd. for use as potential anticancer agents. The complexes synthesized include [{cis-PtCl2(NH3)}2(.mu.-dpzm)], [{trans-PtCl2(Me2SO)}2(.mu.-dpzm)] and

[{cis-PtCl2(Me2SO)}2(.mu.-dpzm)]. The characterization of these complexes

is based on microanal., IR and 1H NMR data.

174585-20-7P

SOURCE:

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and IR spectra and anticancer activity)

RN 174585-20-7 CAPLUS

CN Platinum, diamminetetrachloro[.mu.-[4,4'-methylenebis[1H-pyrazole]-N2:N2']]di-, stereoisomer (9CI) (CA INDEX NAME)

L22 ANSWER 18 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1995:268087 CAPLUS

DOCUMENT NUMBER:

TITLE:

Ammine/amine platinum(II) complexes effective in vivo

against murine tumors sensitive or resistant to

cisplatin and tetraplatin

AUTHOR(S):

Siddik, Zahid H.; Thai, Gerald; Yoshida, Motofumi;

Zhang, Yan-Ping; Khokhar, Abdul R.

CORPORATE SOURCE:

M.D. Anderson Cancer Center, University of Texas,

Houston, TX, 77030, USA

SOURCE:

J. Cancer Res. Clin. Oncol. (1994), 120(10), 571-7

CODEN: JCROD7; ISSN: 0171-5216

DOCUMENT TYPE:

LANGUAGE:

Journal English

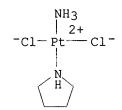
AB Three homologous series, each differing from the other in the coordinated amine ligand class, namely alicyclic, heterocyclic or isoaliph., were highly effective against wild-type murine leukemia L1210/0 cells in vivo (T/C = 171%-426% at optimal doses). Of the 13 complexes comprising the three series, 3 were inactive in the cisplatin-resistant L1210/DDP model, but the other 10 maintained good efficacy (T/C = 131%-167%). Long-term survivors, frequently obsd. with these complexes in the L1210/0 model, were also seen in the L1210/DDP model but to a lesser extent. In the homologous alicyclic series, which contained six analogs, as the alicyclic ring size increased, potency against L1210/0 and L1210/DDP cells also increased up to cyclohexylamine, and then declined. Four ammine/alicyclic amine analogs were evaluated against L1210/DACH cells, which are cross-resistant to tetraplatin, and the clin. predictive M5076 reticulosarcoma. Although the congeners were ineffective or minimally effective in prolonging the survival time of L1210/DACH-bearing mice (T/C = 111%-134%), 20%-40% cure rate was consistently obsd. and suggested that the compds. possessed a low inherent ability to circumvent resistance in these tumor cells also. In the solid M5076 model, activity was greatest (tumor growth delays of about 25 days) for the alicyclic homologs contg. the ammine/cyclobutylamine or ammine/cyclopentylamine carrier ligand combination. In summary, ammine/amine platinum (II) analogs have demonstrated promise at the preclin. level in their ability to circumvent acquired resistance, which is a major drawback of cisplatin use in treating cancer.

ΙT 116219-26-2 116235-96-2

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ammine/amine platinum(II) complexes effective in vivo against murine

tumors sensitive or resistant to cisplatin and tetraplatin) RN 116219-26-2 CAPLUS Platinum, amminedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME) CN

RN 116235-96-2 CAPLUS Platinum, amminedichloro(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME) CN



ANSWER 19 OF 63 CAPLUS COPYRIGHT 2001 ACS

1995:228472 CAPLUS CESSION NUMBER:

DOCUMENT NUMBER: 122:31730

TITLE:

Circumvention of platinum resistance:

structure-activity relationship for homologous series of ammine/amine platinum(II) complexes in L1210 cell

AUTHOR(S): Yoshida, Motofumi; Khokhar, Abdul R.; Siddik, Zahid H.

CORPORATE SOURCE: Dep. Clin. Investigation, Univ. Texas M.D. Anderson

Cancer Cent., Houston, TX, 77030, USA

SOURCE: Anti-Cancer Drug Des. (1994), 9(5), 425-34

CODEN: ACDDEA; ISSN: 0266-9536

DOCUMENT TYPE: Journal

LANGUAGE: English

Ammine/amine dichloroplatinum(II) complexes have been evaluated for structure-activity relation in wild-type L1210/0, 185-fold cisplatin-resistant L1210/DDP and 39-fold tetraplatin-resistant L1210/DACH murine leukemia cells. The mechanism of resistance in these cell lines is multifactorial, with DNA repair playing a dominant role. The amines incorporated in the complexes were selected from the alicyclic, heterocyclic and isoaliph. class, and contained 3, 4, 5 or 6 carbon atoms. The studies demonstrated that ascending each of the homologous series increased cytotoxic potency against sensitive and cisplatin-resistant cell lines and, more importantly, reduced the cross-resistance of cisplatin-resistant cells. Resistance factors (IC50 in resistant cells/IC50 in wild-type cells) were substantially lower than those for cisplatin, but greater than those seen for tetraplatin. In L1210/DACH cells, the potency remained similar across the alicyclic and isoaliph. series, while there was a consistent decrease in activity in the heterocyclic series for each stepwise increase in amine size. Furthermore, the relation between structure and resistance factor in L1210/DACH cells was in direct contrast to that seen in the L1210/DDP

model in that the factors increased on ascending the homologous series stepwise. The lower members of the alicyclic and heterocyclic series and cisplatin had comparable resistance factors in the L1210/DACH line; higher members displayed resistance factors that were comparable to or greater than that of tetraplatin. These results provide evidence for amine class and size as factors that can modulate the potency and capacity of ammine/amine platinum complexes to circumvent cisplatin or tetraplatin

IT 116219-26-2 116235-96-2

> RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (circumvention of platinum resistance and structure-activity relationship for homologous series of ammine/amine platinum(II) complexes)

RN 116219-26-2 CAPLUS

CN Platinum, amminedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-96-2 CAPLUS

CN Platinum, amminedichloro(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

ANSWER 20 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:123362 CAPLUS

DOCUMENT NUMBER: 120:123362

TITLE: Structures of the nitroimidazole platinum group metal

> complexes: cis-amminedibromo[1-({[(2hydroxyethyl) amino] carbonyl } methyl) -2-

nitroimidazole]platinum(II) and trans-dichlorobis(1hydroxyethyl-2-methyl-5-nitroimidazole)palladium(II)

AUTHOR(S): Rochon, Fernande D.; Melanson, Robert; Farrell,

Nicholas

CORPORATE SOURCE: Dep. Chem., Univ. Quebec, Montreal, PQ, H3C 3P8, Can.

SOURCE: Acta Crystallogr., Sect. C: Cryst. Struct. Commun.

(1993), C49(10), 1703-6

CODEN: ACSCEE; ISSN: 0108-2701

DOCUMENT TYPE: Journal LANGUAGE: English

AB Cis-[PtBr2L(NH3)] (L = N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide (etanidazole)) was prepd. and crystd. in orthorhombic, space group Pnca, Z = 8, R = 0.062. Pt has a square-planar coordination. The Pt-Br bond

trans to the nitroimidazole ligand is slightly shorter [2.375 (3) .ANG.] than the Pt-Br bond trans to NH3 [2.397 (3) .ANG.]. The dihedral angle between the Pt coordination plane and the imidazole ring is 69.1.degree., while the nitro group makes an angle of 32.degree. with the imidazole ring plane. The structure is stabilized by the hydrogen bonding of the NH3 ligands and the hydroxyl groups. The crystal structure was also detd. for trans-[PdCl2L'2] (L' = 2-methyl-5-nitroimidazole-1-ethanol (metronidazole)) monoclinic, space group P21/c, Z = 2, R = 0.027. The bond distances Pd-Cl = 2.297 (1) and Pt-N = 2.007 (2) .ANG.. The dihedral angle between the Pd coordination plane and the imidazole ring is 88.6 (1).degree., while the nitro groups make an angle of 3.9(3).degree. with the imidazole plane. The structure is stabilized by hydrogen bonding between the hydroxyl groups and the chloro ligands.

ΤT 152837-74-6P

> RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

152837-74-6 CAPLUS RN

CN Platinum, amminedibromo[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1acetamide-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

ANSWER 21 OF 63 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1994:152111 CAPLUS

DOCUMENT NUMBER: 120:152111

TITLE: Formation and x-ray crystal structure analysis of a platinum(IV) complex of 1-methylthymine, obtained

through gold(III) treatment of a Pt(II) complex Renn, Oliver; Lippert, Bernhard; Albinati, Alberto;

AUTHOR(S): Lianza, Francesca

CORPORATE SOURCE: Fachbereich Chemie, Universitaet Dortmund, Dortmund,

D-44221, Germany

Inorg. Chim. Acta (1993), 211(2), 177-82 SOURCE:

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal

LANGUAGE: English

The prepn. and crystal structure of cis, cis-[(NH3)2Pt(1-MeT)2(OH)(H2O)]AuCl4.H2O (I; 1-MeTH = 1-methylthymine) is reported. I contains both heterocyclic bases bound to Pt via the N3 positions, the 2 nucleobase ligands being in a head-to-head orientation. I crystallizes as triclinic, space group P.hivin.1, a 8.435(4), b 11.884(3), c 12.869(7) .ANG., .alpha. 97.28(3), .beta. 91.66(5), .gamma. 110.66(5).degree., Z =

2, R = 0.056, Rw = 0.065.

ΙT 151591-41-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and crystal structure and IR and XPS spectra of)

RN 151591-41-2 CAPLUS

CN Platinum(1+), diammineaquabis(1,5-dimethyl-2,4(1H,3H)-pyrimidinedionato-N3)hydroxy-, (OC-6-24)-, (SP-4-1)-tetrachloroaurate(1-), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 151591-40-1

CMF C12 H23 N6 O6 Pt . Au C14

> 2_ CM

CRN 151591-39-8

CMF C12 H23 N6 O6 Pt

CCI CCS

CDES 7:0C-6-24

CM 3

CRN 14337-12-3 CMF Au Cl4

CCI CCS

CDES 7:SP-4-1

ANSWER 22 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1993:182182 CAPLUS

DOCUMENT NUMBER:

118:182182

TITLE:

Trans-platinum compounds with anti-tumor activity,

their preparation, and compositions containing them

INVENTOR(S): Barnard, Christopher Francis James

PATENT ASSIGNEE(S):

Johnson Matthey PLC, UK

SOURCE:

Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 503830 R: AT, BE,	A1 CH, DE	19920916 , DK, ES, F		19920304 NI. PT SE
CA 2061759	AA	19920910	CA 1992-2061759	19920224
AU 9211419	A1	19920910	AU 1992-11419	19920303
AU 641850	B2	19930930		
NO 9200894	A	19920910	NO 1992-894	19920306
FI 9201021	A	19920910	FI 1992-1021	19920309
HU 60747	A2	19921028	HU 1992-793	19920309
JP 04327596	A2	19921117	JP 1992-50519	19920309
ZA 9201737	A	19921125	ZA 1992-1737	19920309
US 5194645	A	19930316	US 1992-848681	19920309
PRIORITY APPLN. INFO	.:		GB 1991-5037	19910309
OTHER SOURCE(S):	MAI	RPAT 118:18	2182	

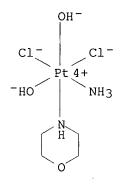
Trans-Pt(IV) compds. of general formula [PtX2Y2L1L2)], where X is halogen; Y is halogen, hydroxyl, or carboxylate; and each L is an amine ligand, providing L1 and L2 are not both NH3, are surprisingly active against cancer cells, in contrast to expectations that all trans-Pt compds. are inactive. Specific claimed compds. are trans-[PtCl2(OH)2(NH3)(c-C6H9NH2)], trans-[PtCl2(OH)2(NH3)(c-C6H11NH2)], trans-[PtCl2(OH)2(NH3)((CH3)2CHNH2)], trans-[PtCl2(OH)2(NH3)((CH3)3CNH2)], and trans-[PtCl2(OCOCH3)2(NH3)(c-C6H11NH2)], where c indicates a cyclic compd.

IT 146924-17-6P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as antitumor pharmaceutical)

RN 146924-17-6 CAPLUS

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-12)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1992:187485 CAPLUS

DOCUMENT NUMBER: 116:187485

DOCUMENT NUMBER: 110:10/405

TITLE: Ammine/amine platinum(IV) dicarboxylates: a novel class of platinum complex exhibiting selective cytotoxicity to intrinsically cisplatin-resistant

human ovarian carcinoma cell lines

AUTHOR(S): Kelland, Lloyd R.; Murrer, Barry A.; Abel, George;

Giandomenico, Christen M.; Mistry, Prakash; Harrap,

Kenneth R.

CORPORATE SOURCE: Drug Dev. Sect., Inst. Cancer Res.,

Belmont/Sutton/Surrey, SM2 5NG, UK

SOURCE: Cancer Res. (1992), 52(4), 822-8

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE:

English

Journal LANGUAGE: AB

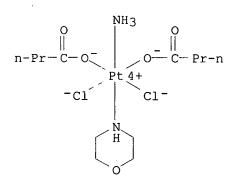
Using a panel of six human ovarian carcinoma cell lines varying by two orders of magnitude in terms of cisplatin cytotoxicity, the authors investigated the in vitro antitumor activity of a series of novel alkylamine ammine dicarboxylatodichloroplatinum (IV) complexes of the general formula c,t,c-[PtCl2(OCOR1)2NH3(RNH2)];R and R1= aliph., arom. or alicyclic. A clear relationship existed between increasing the no. of carbons in the R1 substituent and increasing cytotoxicity up to R1 = C5H11. In terms of changing the R group, max. cytotoxic effects were conferred by alicyclic substituents. Furthermore, increasing the alicyclic ring size from cyclobutane through to cycloheptane resulted in increasing cytotoxicity. The agents with longer axial chains (e.g., JM300, R = cyclohexyl, R1 = C6H13) were more cytotoxic than cisplatin and, moreover, exhibited a selective cytotoxic effect against the most intrinsically cisplatin-resistant cell lines. The carboxylates JM221 (R = cyclohexyl, R1 = C3H7) and JM244 (R = Pr, R1 = C6H5) also retained activity against a 4-fold cisplatin-acquired resistant variant of the 41M cell line. At least part of the increased cytotoxicity of the dicarboxylate, JM221, over cisplatin appeared to be attributable to an increased intracellular accumulation. This novel class of platinum compd. represents a valuable lead in the development of a "third-generation" agent capable of exhibiting activity against clin. disease currently resistant to cisplatin.

ΙT 140430-88-2

> RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor activity of, in cisplatin-resistant human ovarian carcinoma, structure in relation to)

RN 140430-88-2 CAPLUS

CN Platinum, amminebis(butanoato-0)dichloro(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)



L22 ANSWER 24 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

1991:669138 CAPLUS

115:269138

TITLE:

Characterization and properties of monoammine

nitroimidazole complexes of platinum

[PtCl2(NH3)(NO2Im)]. Crystal and molecular structure

of cis-amminedichloro(1-{(((2-

hydroxyethyl)amino)carbonyl)methyl}-2-

nitroimidazole)platinum(II)

AUTHOR(S):

Rochon, Fernande D.; Kong, Pi Chang; Melanson, Robert;

Skov, Kirsten A.; Farrell, Nicholas

Searched by Barb O'Bryen, STIC 308-4291

CORPORATE SOURCE:

Vermont Reg. Cancer Cent., Univ. Vermont, Burlington,

VT, 05405, USA

SOURCE:

Inorg. Chem. (1991), 30(24), 4531-5

CODEN: INOCAJ; ISSN: 0020-1669

Journal

DOCUMENT TYPE: English LANGUAGE:

The characterization of [PtCl2(NH3)(NO2Im)] (NO2Im = Etanidazole (L), Misonidazole (L1) and Metronidazole (L2)) is reported. Both cis and trans isomers may be isolated for the L1 and L2 complexes. The crystal structure of cis-[PtCl2(NH3)L] has been detd. by x-ray diffraction. crystals are orthorhombic, space group Pnab with a 14.867(7), b 9.915(5), c 19.015(9) .ANG., Z = 8, R = 0.062 and Rw = 0.052. Platinum has the expected square-planar coordination. The Pt-Cl bond trans to the nitroimidazole ligand is shorter (2.269(3) .ANG.) than normal. The dihedral angle between the platinum plane and the imidazole ring is 111.degree., while the nitro group makes an angle of 31.degree. with the imidazole ring plane. Electrochem. and 195Pt NMR data are also reported. The relevance of the chem. properties to their biol. properties as radiosensitizers and hypoxic cytotoxins is discussed.

IT

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure and electrochem. redn. and radiosensitizing and hypoxic cytotoxin properties of)

RN 136844-76-3 CAPLUS

Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-CN acetamide-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

Some as matters

ΙT 114532-23-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and electrochem. redn. and radiosensitizing and hypoxic cytotoxin properties of)

RN 114532-23-9 CAPLUS

Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-CN ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

IT 110321-22-7P 112198-62-6P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and isomerization and electrochem. redn. and radiosensitizing and hypoxic cytotoxin properties of)

RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{NH3} \\ & 2+ \\ -\text{Cl-Pt} & \text{Cl-} \\ & \\ & \\ & \\ \text{O}_2\text{N} & \text{CH}_2-\text{CH}_2-\text{OH} \end{array}$$

RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

NH3 .
$$-C1-Pt \xrightarrow{N} C1-V = C1-$$

IT 121350-06-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. by isomerization and electrochem. redn. and radiosensitizing and hypoxic cytotoxin properties of)

RN 121350-06-9 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 AUSWER 25 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1991:669081 CAPLUS

DOCUMENT NUMBER:

115:269081

TITLE:

A tetranuclear tervalent platinum complex with

.alpha.-pyrrolidonate and deprotonated ammine bridging ligands, [(NO3)(NH3)2Pt(III)(C4H6NO)2Pt(III)(NH3)(.mu.-

NH2)]2(NO3)4

AUTHOR(S):

Matsumoto, Kazuko; Harashima, Kazuo

CORPORATE SOURCE:

Dep. Chem., Waseda Univ., Tokyo, 169, Japan

SOURCE:

AR

Inorg. Chem. (1991), 30(15), 3032-4

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE:

Journal English

LANGUAGE:

From the reaction of [PtII2PtIII2(NH3)8 (.mu.-L)](NO3)6.cntdot.2H2O (HL = .alpha.-pyrrolidone) with excess pyrazine in water were obtained dark green, almost black block crystals of [(NO3)(NH3)2PtIII(.mu.-L)2PtIII(NH3)(.mu.-NH2)]2(NO3)4. The crystal is monoclinic (P2/c) with cell a 10.652(5) b 18.512(7) c 10.430(4) .ANG., .beta. 102.42(3).degree., Z = 2, and V = 2008(1) .ANG.3. The complex consists of two .alpha.-pyrrolidonate-bridged Pt(III) dimeric units. The two dimers are bridged by two NH2- ligands to form tetranuclear [(NO3)(NH3)2PtIII(.mu.-L) 2PtIII (NH3) (.mu.-NH2)] 24+. The Pt-Pt distance in the dimeric unit is 2.608(1) .ANG., whereas that of the interdimer sepn. is 3.160(2) .ANG..

ΙT 135228-16-9P

> RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

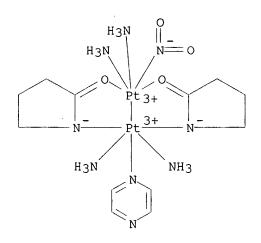
RN 135228-16-9 CAPLUS

CN Platinum(3+), tetraammine(nitrito-N)(pyrazine-N1)bis[.mu.-(2pyrrolidinonato-N1:02)]di-, (Pt-Pt), stereoisomer, trinitrate (9CI) INDEX NAME)

CM 1

135228-15-8 CMF C12 H28 N9 O4 Pt2

CCI CCS CDES *



CM

CRN 14797-55-8

CMF N 03



L22 ANSWER 26 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:568093 CAPLUS

DOCUMENT NUMBER: 113:168093

TITLE: Radiosensitization by metal complexes of

4(5)-nitroimidazole

AUTHOR(S): Skov, K. A.; Farrell, N. P.

CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res.

Cent., Vancouver, BC, V5Z 1L3, Can.

SOURCE: Int. J. Radiat. Biol. (1990), 57(5), 947-58

CODEN: IJRBE7

DOCUMENT TYPE: Journal LANGUAGE: English

AB Four closely-related cis-platinum (Pt) complexes of 4(5)-nitroimidazole were examd. with respect to properties of radiobiol. interest, to test the hypothesis that targeting a nitroimidazole (NO2Im) to DNA could enhance its radiosensitizing ability: PtCl2(5-NO2Im)2 (I); PtCl2(4-NO2Im)2 (II); PtCl2(NH3)(5-NO2Im) (III); PtCl2(NH3)(4-NO2Im) (IV). The redn. potential was affected to the same extent on metal binding in all of the complexes (.DELTA.E1/2 = +200 mV, cf. ligand measured polog.). Higher sensitization by 5-NO2 complexes I, III (cf. II, IV) was found. Only the mono complexes III and IV bind to DNA (in an assay using inhibition of restriction endonuclease activity); these radiosensitize as well as, or better than, free ligand in hypoxic CHO cells, and better than the bis complexes (I and The toxicity of the mono complexes is higher than ligand, and parallels the binding (III, IV, mono bis analogs). The complexes are compared with 4-nitroimidazole complexes of Ru, with respect to toxicity, binding, and radiosensitization.

IT 110302-83-5 129784-94-7

RL: BIOL (Biological study)

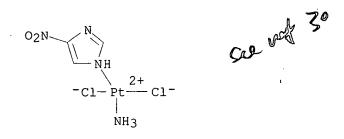
(radiosensitization by, of mammalian cells, DNA binding in relation to)

RN 110302-83-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 129784-94-7 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



ANSWER 27 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:603810 CAPLUS

DOCUMENT NUMBER: 113:203810

TITLE: Coordination chemistry of trans-(H3N)2Pt(II) with

uracil nucleobases. A comparison with cis-(H3N)2Pt(II) Dieter, Iris; Lippert, Bernhard; Schoellhorn, Helmut;

AUTHOR(S): Dieter, Iris Thewalt, Ulf

CORPORATE SOURCE: Fachbereich Chem., Univ. Dortmund, Dortmund, D-4600,

Fed. Rep. Ger.

SOURCE: Z. Naturforsch., B: Chem. Sci. (1990), 45(6), 731-40

CODEN: ZNBSEN; ISSN: 0932-0776

DOCUMENT TYPE: Journal LANGUAGE: English

Protonated and heteronuclear adducts and trans-L2PtX2 (L = NH3, NH2Me, HXAΒ = 1-methyluracil (HQ), or uridine) were prepd. and studied by spectroscopic methods and in 2 cases by x-ray crystallog. trans-(NH3)2PtQ2Ag2(NO3)2H2O.H2O (I) crystd. orthorhombic, space group Pna21, a 13.206(6), b 7.238(9), c 22.051(10) .ANG., Z = 4, R = 0.058, Rw = 1.0080.063. I forms a polymeric structure with PtAg2 entities linked via O(4) sites of th 1-methyluracilato ligands. Pt is coordinated through N(3), the Ag centers have a mixed O(2), O(4) coordination. trans, trans, trans-[(NH3)2Pt(OH)2(HQ)2](NO3)2 (II) contains 2N(3)-bound neutral 1-methyluracil ligands, hence rare tautomers of this model nucleobase. crystallizes monoclinic, space group P21/n, a 7.098(1), b 10.395(1), c 13.295(2) .ANG., .beta. 91.88(2).degree., Z = 2, R = 0.059, Rw = 0.053. While the chem. leading to Pt(IV) oxidn. products from trans-L2PtX2 is similar to that of the cis-isomer, protonation as well as heteronuclear complex formation of trans-L2PtX2 is more difficult to accomplish than

origin.
IT 129700-79-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure and deprotonation and reaction of, with chloride)

with the cis-isomer. This difference appears to be primarily of steric

RN 129700-79-4 CAPLUS

CN Platinum(2+), diamminedihydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedione-.kappa.N3)-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

CRN 129700-78-3 CMF C10 H20 N6 O6 Pt CCI CCS CDES 7:OC-6-12

CM 2

CRN 14797-55-8 CMF N O3

IT 129700-81-8P 129700-83-0P 129700-84-1P

130039-07-5P

RN 129700-81-8 CAPLUS

CN Platinum(1+), diamminedihydroxy(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)(1-methyl-2,4(1H,3H)-pyrimidinedione-N3)-, (OC-6-13)-, nitrate (9CI) (CA INDEX NAME)

CM 1

CRN 129700-80-7 CMF C10 H19 N6 O6 Pt CCI CCS CDES 7:OC-6-13

CM 2

CRN 14797-55-8 CMF N O3

RN 129700-83-0 CAPLUS

CN Platinum, diamminedihydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedionato- \dot{N} 3)-, (OC-6-12)- (9CI) (CA INDEX NAME)

RN 129700-84-1 CAPLUS

CN Platinum, diamminedichlorobis(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)

RN 130039-07-5 CAPLUS

CN Platinum, diamminedichlorobis(5-chloro-1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)

L22 ANSWER 28 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1990:210664 CAPLUS

DOCUMENT NUMBER:

112:210664

TITLE:

Toxicity of [PtCl2(NH3)L] in hypoxia; L = misonidazole

or metronidazole

AUTHOR(S):

Skov, K. A.; Adomat, H.; Chaplin, D. J.; Farrell, N.

Ρ.

CORPORATE SOURCE:

Med. Biophys. Unit, BC Cancer Res. Cent., Vancouver,

BC, V5Z 1L3, Can.

SOURCE:

Anti-Cancer Drug Des. (1990), 5(1), 121-8

CODEN: ACDDEA; ISSN: 0266-9536

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB There is increasing interest in compds. which show selective toxicity to the resistant hypoxic portions of tumors. Cisplatin does not generally show preferential toxicity in hypoxic cells, whereas nitroimidazoles do. It is proposed that attachment of a nitroimidazole could add a degree of hypoxic selectivity to Pt agents. Pt complexes contg. one nitroimidazole ligand bind to DNA and show higher toxicity in hypoxic than aerobic CHO cells. cis And trans isomers of complexes with misonidazole (a

Page 45

2-nitroimidazole) and metronidazole (a 5-nitroimidazole) are compared with respect to binding to DNA (approx. the same), redn. potential (trans miso > cis miso > cis metro > trans metro), and toxicity (trans > cis meso, cis > trans metro, with trans miso .apprx. cis metro in hypoxia, despite significantly different redn. potentials). The effect of platination on nitroimidazole toxicity is not entirely explained by DNA binding and increased redn. potential. These compds. do not exhibit cross resistance with cisplatin in L1210 resistant cells. This factor, their selectivity for hypoxia, and preliminary results in vivo indicating potentiation of antitumor activity by the vasoactive compd., hydralazine, which increases tumor hypoxia, suggest further development of these compds. for use in tumors with resistant hypoxic portions.

TΤ 110321-22-7 112198-62-6 114532-23-9

121350-06-9

RL: PRP (Properties)

(cytotoxicity of, in hypoxia, structure in relation to)

RN 110321-22-7 CAPLUS

Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, CN (SP-4-3)-(9CI) (CA INDEX NAME)

112198-62-6 CAPLUS RN

CNPlatinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114532-23-9 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121350-06-9 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)-(9CI) (CA INDEX NAME)

L22 ANSWER 29 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1990:584699 CAPLUS

DOCUMENT NUMBER:

113:184699

TITLE:

Pt (IV) complexes as antitumor agents

INVENTOR(S):

Abrams, Michael J.; Gaindomenico, Christen M.; Murrer,

Barry A.; Vollano, Jean F. Johnson Matthey, Inc., USA

SOURCE:

PATENT ASSIGNEE(S):

Eur. Pat. Appl., 21 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 328274	A1	19890816	EP 1989-300787	19890127
EP 328274	B1	19941019		
R: AT, BE,	CH, DE	, ES, FR, GB,	GR, IT, LI, LU, NL	, SE
ES 2063119	Т3	19950101	ES 1989-300787	19890127
IL 89119	A1	19940412	IL 1989-89119	19890130
AU 8928971	A1	19890803	AU 1989-28971	19890201
AU 618310	B2	19911219		
CA 1340286	A1	19981222	CA 1989-589796	19890201
DK 8900491	Α	19890803	DK 1989-491	19890202
FI 8900512	Α	19890803	FI 1989-512	19890202
FI 91260	В	19940228		
FI 91260	С	19940610		
NO 8900426	Α	19890803	NO 1989-426	19890202
NO 177569	В	19950703		

NO 177569	С	19951011		
JP 01294684	A2	19891128	JP 1989-24751	19890202
HU 49890	· A2	19891128	ни 1989-522	19890202
HU 205767	В	19920629	•	•
ZA 8900831	А	19891227	ZA 1989-831	19890202
US 5072011	A	19911210	US 1990-602931	19901025
US 5244919	Α	19930914	US 1991-723971	19910701
PRIORITY APPLN. INF	0.:		US 1988-151674	19880202
			US 1989-296776	19890113
			US 1990-602931	19901025

OTHER SOURCE(S): MARPAT 113:184699

AB Pt(IV) complexes, AA1 Pt(OCOR1)2X2 where A, A1 = NH3 or NH2, R, R1 = H, alkyl, alkenyl, aryl, aralykyl, alkylamino, or alkoxy or their derivs., and X = halogen or alkylmono- or -dicarboxylate as antitumor agents. Many of these complexes are sol. in both water and org. solvents, and this dual soly. might contribute to the high antitumor activity. Thus, cis-trans-cis-PtCl2(O2CH)2NH3(cyclohexylamine) was prepd. by formylation of cis-trans-cis-PtCl2(OH)2NH3(cyclohexyl-NH2) in HCOOH during heating at 50.degree. The antitumor activity of some of these compds. was demonstrated and their LD50 and ED90 values (i.p. and oral) are tabulated.

IT 129598-45-4P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of, as antitumor agent)

RN 129598-45-4 CAPLUS

CN Platinum, bis(acetato-O)amminedichloro(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)

L22 ANSWER 30 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:453447 CAPLUS

DOCUMENT NUMBER: 111:53447

TITLE: Platinum(II) complexes with one radiosensitizing

ligand useful in tumor therapy

INVENTOR(S): Skov, Kirsten A.; Farrell, Nicholas P.; Chaplin, David

J.

PATENT ASSIGNEE(S): British Columbia Cancer Foundation, Can.

SOURCE: Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

```
EP 287317
                       A2
                            19881019
                                                            19880412
                                           EP 1988-303258
     EP 287317
                      A3
                            19890208
         R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
                            19900501
     US 4921963
                       A
                                          US 1987-37498
                                                            19870413
     JP 01052788
                       A2
                            19890228
                                                            19880413
                                           JP 1988-92608
                            19920421
     CA 1299179
                       A1
                                           CA 1988-564082
                                                            19880413
     US 5026694
                                           US 1989-374356
                                                            1.98.90.630
                       Α
                            19910625
PRIORITY APPLN. INFO.:
                                        US 1987-37498
                                                            19870413
OTHER SOURCE(S):
                         MARPAT 111:53447
AB
     Square planar Pt(II) complexes are described of the formula [PtX2(NR2H)L]
     (I) or [PtX(NR2H)2L]+Y- (II) [X, Y-=a monovalent biol. acceptable anion
     (X2 in I may also be a divalent biol. acceptable anion); R = H or C1-8
     alkyl; R2 = a morpholino or piperidino residue; L = a radiosensitizing
     mononitro-substituted arom. ligand with .gtoreq.1 heterocyclic N and/or
     substituent amine]. These complexes bind to DNA and sensitize hypoxic
     tumors to radiation; they are useful chemotherapeutic agents. cis-I (R =
     H; X = Cl; L = misonidazole) (cis-III) was prepd. by reaction of 1 equiv
     of misonidazole with K[PtCl3(NH3)] and treatment of the residue with Et2O.
     Treatment of cis-III with EtOH yielded trans-III. Chinese hamster ovary
     cells were incubated with III (100 .mu.mol/dm3) for 1 h at 37.degree. to
     allow binding to DNA prior to radiation. By use of a known method,
     radiosensitization of the cells was obsd.
ΙT
     110302-83-5 110321-22-7 112198-62-6
     114532-23-9 121281-51-4 121350-02-5
     121350-03-6 121350-04-7 121350-05-8
     121350-06-9 121350-07-0 121668-91-5
     121668-92-6 121703-32-0 121703-33-1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (as radiosensitizer, for neoplasm treatment)
RN
     110302-83-5 CAPLUS
CN
     Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA
     INDEX NAME)
```

RN 110321-22-7 CAPLUS CN Platinum, amminedichloro(2-m

Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114532-23-9 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121281-51-4 CAPLUS

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121350-02-5 CAPLUS

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]- (9CI) (CA INDEX NAME)

RN 121350-03-6 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)(9CI) (CA INDEX NAME)

RN 121350-04-7 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]- (9CI) (CA INDEX NAME)

RN 121350-05-8 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)- (9CI) (CA INDEX NAME)

RN 121350-06-9 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA'INDEX NAME)

RN 121350-07-0 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121668-91-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)- (9CI) (CA INDEX NAME)

RN 121668-92-6 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)- (9CI) (CA INDEX NAME)

RN 121703-32-0 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121703-33-1 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1988:521599 CAPLUS

DOCUMENT NUMBER:

109:121599

TITLE:

Preparation of ammine heterocyclyl platinum complexes

as antitumor agents

INVENTOR(S):

Totani, Tetsushi; Aono, Katsutoshi; Adachi, Yasuko

PATENT ASSIGNEE(S): Shionogi and Co., Ltd., Japan

SOURCE:

Eur. Pat. Appl., 22 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 273315 EP 273315	A1 B1	19880706 19920318	EP 1987-118819	19871218
R: AT, BE,	CH, DE	, ES, FR, GB	, GR, IT, LI, LU, NL	, SE
JP 63264492	A2	19881101	JP 1987-321977	19871218
US 4902797	A	19900220	US 1987-135061	19871218
AT 73814	Ε	19920415	AT 1987-118819	19871218
ES 2032430	Т3	19930216	ES 1987-118819	19871218
CA 1327039	A1	19940215	CA 1987-554853	19871218
PRIORITY APPLN. INFO	.:		JP 1986-303529	19861218
			EP 1987-118819	19871218

OTHER SOURCE(S):

MARPAT 109:121599

GI For diagram(s), see printed CA Issue.

AB Title compds I (R = alkyl OH carbo

AB Title compds. I (R = alkyl, OH, carboxy, alkoxy, halo, oxo; m = 2-7; X, Y = Cl, NO3; XY = carboxylate) are prepd. as antitumor agents. An aq. soln.

of (ammine) (piperidine) platinum (II) nitrate was ion-exchanged to give the corresponding hydroxide, which was treated with glycolic acid to give 20% (ammine) (piperidine) platinum glycolate, which proved quite effective against cisplatin-resistant L1210 leukemia.

116219-17-1P 116219-18-2P 116219-19-3P 116219-20-6P 116219-21-7P 116219-22-8P 116219-23-9P 116219-24-0P 116219-25-1P 116219-26-2P 116219-27-3P 116219-28-4P

116219-29-5P 116219-30-8P 116219-31-9P 116235-96-2P 116297-79-1P 116297-80-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as antitumor agent)

RN 116219-17-1 CAPLUS

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-18-2 CAPLUS

CN Platinum, amminebis(nitrato-O)(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-19-3 CAPLUS

CN Platinum, ammine[ethylpropanedioato(1-)-0,0'](pyrrolidine)-, (SP-4-3)(9CI) (CA INDEX NAME)

RN 116219-20-6 CAPLUS

CN Platinum, ammine[ethanedioato(2-)-0,0'](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-21-7 CAPLUS

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2](pyrrolidine)-, (SP-4-4)- (9CI) (CA INDEX NAME)

RN 116219-22-8 CAPLUS

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-23-9 CAPLUS

CN Platinum, amminebis(nitrato-O)(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-24-0 CAPLUS

CN Platinum, ammine[ethylpropanedioato(2-)-0,0'](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-25-1 CAPLUS

CN Platinum, ammine[ethanedioato(2-)-0,0'](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-26-2 CAPLUS

CN Platinum, amminedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-27-3 CAPLUS

CN Platinum, ammine[hydroxyacetato(2-)-01,02](piperidine)-, (SP-4-3)- (9CI)

(CA INDEX NAME)

RN 116219-28-4 CAPLUS

CN Platinum, amminedichloro(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-29-5 CAPLUS

CN Platinum, amminebis(nitrato-O)(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-30-8 CAPLUS

CN Platinum, amminedichloro(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-31-9 CAPLUS

CN Platinum, amminebis(nitrato-O)(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-96-2 CAPLUS

CN Platinum, amminedichloro(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116297-79-1 CAPLUS

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116297-80-4 CAPLUS

CN Platinum, ammine[hydroxyacetato(2-)-01,02](piperidine)-, (SP-4-4)- (9CI) (CA INDEX NAME)

IT 116219-32-0P 116219-33-1P 116235-97-3P

116235-98-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as antitumor agent intermediate)

116219-32-0 CAPLUS

CN Platinum, amminediiodo(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN

RN 116219-33-1 CAPLUS

CN Platinum, amminediiodo(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX

NAME)

RN 116235-97-3 CAPLUS

CN Platinum, amminediiodo(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-98-4 CAPLUS

CN Platinum, amminechloroiodo(3-pyrrolidinol-N1)- (9CI) (CA INDEX NAME)

L22 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1988:215259 CAPLUS

DOCUMENT NUMBER: 108:215259

TITLE: Synthesis and characterization of new platinum(II)

complexes containing thiazole and imidazole donors

AUTHOR(S): Muir, Mariel M.; Cadiz, Mayra E.; Baez, Adriana

CORPORATE SOURCE: Dep. Chem., Univ. Puerto Rico, Rio Piedras, 00932, P.

SOURCE: Inorg. Chim. Acta (1988), 151(3), 209-13

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal LANGUAGE: English

cis-Pt(NH3)LCl2 (L = thiazole, 2-bromothiazole, benzothiazole, 2,1,3-benzothiadiazole, 1,2,3-benzothiadiazole, imidazole,

1-methylimidazole) were prepd. The complexes were characterized by IR and UV-visible spectroscopy, 1H NMR and elemental analyses. The thiazoles and

benzothiazoles were coordinated through the N heteroatom. Both the

benzothiadiazoles were coordinated through S. Several of the complexes showed significant cytotoxic activity.

IT 114487-35-3P 114502-44-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and cytotoxic activity of)

RN 114487-35-3 CAPLUS

CN Platinum, ammine(2-bromothiazole-N3)dichloro-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114502-44-2 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

IT 114487-38-6P 114487-39-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

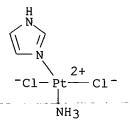
(prepn. of)

RN 114487-38-6 CAPLUS

CN Platinum, amminedichloro(1-methyl-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114487-39-7 CAPLUS

CN Platinum, amminedichloro(1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



L22 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1988:108927 CAPLUS

DOCUMENT NUMBER:

108:108927

TITLE:

Radiosensitizers targeted to DNA using platinum. Synthesis, characterization, and DNA binding of

cis-[PtCl2(NH3)(nitroimidazole)]

AUTHOR(S): CORPORATE SOURCE: Farrell, Nicholas; Skov, Kirsten A.

SOURCE:

Dep. Chem., Univ. Vermont, Burlington, VT, 05405, USA J. Chem. Soc., Chem. Commun. (1987), (13), 1043-4

CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE:

Journal

LANGUAGE:

English

GΙ

$$NH_2$$
 $N-P-C1$
 O_2N
 R_1
 T

The prepn. and characterization of cis-[PtCl2(NH3)(misonidazole)] (I; R = CH2CH(OH)CH2OMe, R' = NO2) and cis-[PtCl2(NH3)(metronidazole)] (I; R = CH2CH2OH, R' = Me) are described and their binding to DNA and radiosensitizing activity were examd. Both complexes showed considerable DNA binding and had greater radiosensitizing activity then their bis analogs. The results indicate that radiosensitizing ligands can be targeted to DNA by complexation with Pt.

IT 110321-22-7P 112198-62-6P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and DNA binding and radiosensitizing efficacy of)

RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

CAPLUS COPYRIGHT 2001 ACS L22 ANSWER 34 OF 63

1988:71355 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 108:71355

Platinum complexes with one radiosensitizing ligand TITLE:

[PtCl2(NH3) (sensitizer)]: radiosensitization and

toxicity studies in vitro

AUTHOR(S): Skov, Kirsten A.; Farrell, Nicholas P.; Adomat, Hans

CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res.

> Cent., Vancouver, BC, V5Z 1L3, Can. Radiat. Res. (1987), 112(2), 273-82

CODEN: RAREAE; ISSN: 0033-7587

DOCUMENT TYPE: Journal English LANGUAGE:

SOURCE:

AB Complexes of general formula [PtCl2(NH3)L] with 1 radiosensitizing ligand per Pt are compared with ligand L alone, complexes with 2 radiosensitizers per Pt [PtC12L2], and their analogs with NH3 ligands, with respect to radiosensitizing properties and toxicity in CHO cells. Radiosensitizing ligands, L, were misonidazole, metronidazole, 4(5)-nitroimidazole, and 2-amino-5-nitrothiazole, and the ammine analogs were cis- and trans-DDP [diamminedichloroplatinum(II)] and the monoammine, K[PtCl3(NH3)]. Results are related to a previous study on plasmid DNA binding by these series. The toxicity of the mono series [PtCl2(NH3)L], attributable to DNA binding, is much higher than the corresponding bis complexes, [PtCl2L2]. For L = misonidazole, toxicity is similar to the monoammine, but higher in hypoxic than in aerobic cells. trans-[PtCl2(NH3)-(misonidazole)] is more toxic than the cis isomer. Except for L = 4(5)-nitroimidazole, the complexes [PtCl2(NH3)L] are more toxic than L inm air and hypoxia. Hypoxic radiosensitization by the mono complexes is comparable to the monoammine and is not better than free sensitizers, again except for L =4(5)-nitroimidazole. Significantly lower sensitization is obsd. in oxic

cells. The bis complexes [PtCl2L2], which do not bind to DNA as well as the mono complexes, are less effective radiosensitizers and less toxic than the [PtCl2(NH3)L] series.

IT 110302-83-5 110321-22-7 110321-23-8

112198-62-6 114532-23-9

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (radiosensitizing activity and toxicity of, in CHO cells)

RN 110302-83-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 110321-23-8 CAPLUS

CN Platinum, amminedichloro(5-nitro-2-thiazolamine-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114532-23-9 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 ANSWER 35 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1987:529989 CAPLUS

DOCUMENT NUMBER: 107:129989

TITLE: Assessment of DNA binding of platinum-radiosensitizer

complexes by inhibition of restriction enzymes

AUTHOR(S): Skov, Kirsten A.; Adomat, Hans; Konway, Desmond C.;

Farrell, Nicholas P.

CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res.

Cent., Vancouver, BC, V5Z 1L3, Can.

SOURCE: Chem.-Biol. Interact. (1987), 62(2), 117-29

CODEN: CBINA8; ISSN: 0009-2797

DOCUMENT TYPE: Journal LANGUAGE: English

AB A simple and rapid method has been used to compare the binding of Pt complexes to DNA, in a relatively qual. manner. A compd. bound at or near the restriction site inhibits enzymic cleavage of DNA; inhibition of BamHI and EcoRI activities by complexes was assessed in this study using linearized pSV2-gpt plasmid. The particular interest was in DNA binding by complexes of Pt with known org. radiosensitizers (RS), to det. whether the Pt was able to target the RS to the DNA. Although the PT-RS complexes investigated themselves have moderate radiosensitizing ability (like the inorg. complexes, cis- or trans-DDP), none of the Pt-RS inhibit to the same extent as cis- or trans-DDP. However, there appears to be some correlation between enhanced radiosensitization by Pt-RS over Pt(RS)2, with the degree of Pt binding (as assessed by the assay). The results using isolated DNA suggest that not all complexes bind well (e.g., Pt with 2 RS ligands), but that in certain cases (e.g., Pt with only 1 RS), it is possible to target the drug to the DNA. An ammine or amine ligand may be

required to target a radiosensitizer to DNA using Pt. IT 110302-83-5 110321-21-6 110321-22-7

110321-23-8

RL: BIOL (Biological study)

(DNA binding of, restriction enzymes inhibition in assessment of, radiosensitization in relation to)

RN 110302-83-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA

INDEX NAME)

RN 110321-21-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 110321-23-8 CAPLUS

CN Platinum, amminedichloro(5-nitro-2-thiazolamine-N3)-, (SP-4-3)- (9CI) (CF INDEX NAME)

L22 ANSWER 36 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:466445 CAPLUS

DOCUMENT NUMBER: 105:66445

TITLE: Platinum coordination compounds for linking to

monoclonal antibodies

INVENTOR(S): Heffernan, James Gerard; Hydes, Paul Cedric; Picker,

Donald Harold

PATENT ASSIGNEE(S): Johnson Matthey PLC, UK

SOURCE: Eur. Pat. Appl., 30 pp.

CODEN: EPXXDW DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-			
EP 167310	A2	19860108	EP 1985-304131	19850611
EP 167310	А3	19860423		
EP 167310	В1	19910529		
R: AT, BE,	CH, DE,	, FR, GB, IT,	LI, LU, NL, SE	
AT 63919	E	19910615	AT 1985-304131	19850611
AU 8543930	A1	19870108	AU 1985-43930	19850621
AU 583827	В2	19890511		
JP 61083194	A2	19860426	JP 1985-138046	19850626
JP 06062654	B4	19940817		
CA 1283750	A1	19910430	CA 1985-485669	19850627
US 4760155	A	19880726	US 1986-873130	19860611
US 4956454	A	19900911	US 1988-184140	19880421
PRIORITY APPLN. INFO.	:	U	S 1984-625251	19840627
		E	P 1985-304131	19850611
		U	S 1986-873130	19860611

Pt compds. YR1NHR2PtX2NH2R, e.g., H3NPtCl2R3, R3 = NH2(CH2)3Co2Et, p-H2NC6H4CO2H, morpholino, HOCH2CMe2NH2, HOCH2CH2NH2, etc., were prepd. for linking to monoclonal antibodies to provide a moiety which stabilizes the antibodies to in vivo hydrolysis and localizes the pharmacol. activity, i.e. targeting of the drug. A soln. of K[PtCl3(NH3)] was treated with a soln. of H2N(CH2)3CO2Et.cntdot.HCl and K2CO3 to give PtCl2NH3[NH2(CH2)3CO2Et]. This compd. and PtCl2NH3[NH2C6H4OH-m] gave therapeutic indexes (LD50/ED90) of 4.7 and 2.5 orally when tested against ADJ/PC6 tumor in Balb/C mice.

IT 103436-53-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with silver nitrate and hydrochloric acid)

RN 103436-53-9 CAPLUS

CN Platinum, amminediiodo(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

IT 103436-43-7P 103436-44-8P

RL: PREP (Preparation)

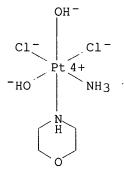
(prepn. of, for linking to monoclonal antibodies, for drug delivery)

RN 103436-43-7 CAPLUS

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 103436-44-8 CAPLUS

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)



L22 ANSWER 37 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1986:563817 CAPLUS

DOCUMENT NUMBER:

105:163817

TITLE:

Metal-stabilized rare tautomers of nucleobases. 1. Iminooxo form of cytosine: formation through metal migration and estimation of the geometry of the free

tautomer

AUTHOR(S):

SOURCE:

Lippert, Bernhard; Schoellhorn, Helmut; Thewalt, Ulf Inst. Anorg. Anal. Chem., Univ. Freiburg, Freiburg,

CORPORATE SOURCE:

7800, Fed. Rep. Ger.

J. Am. Chem. Soc. (1986), 108(21), 6616-21

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE:

Journal

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE:

English

A way is presented for estg. the geometry or rare nucleobase tautomers by AΒ (i) prepg. metal complexes of the rare tautomers, (ii) detg. the crystal structure of the metal complex as accurately as possible, and (iii) subtracting the effect of the metal on the ligand geometry. The prepn., crystal structures, and spectroscopic (1H NMR, Raman) properties are reported of 2 modifications of trans, trans-[Pt(NH3)2(OH)2(1-MeC)2].2H2O (I; 1-MeC = 1-methylcytosine). Neutral 1-MeC ligands are coordinated to Pt through the deprotonated exocyclic N4' positions with N3 protonated. Thus the 1-MeC ligands are in the rare iminooxo tautomer form of cytosine. Modification A of I crystallizes in the triclinic space group P.hivin.1 with a 5.819(2), b 7.178(2), c 13.626(7) .ANG., .alpha. 90.72(4), .beta. 105.82(3), .gamma. 94.02(8).degree., Z = 1, R = 0.020, Rw(F) = 0.020 for 1911 independent reflections. Modification B of I crystallizes in the monoclinic space group P21/c with a 8.892(1), b 11.496(1), c 11.010(1) .ANG., .beta. 100.05(2).degree., Z = 2, R = 0.040, Rw(F) = 0.045 for 2525 independent reflections. The geometries of the 1-MeC ligands in A and B differ from that of the normal, uncomplexed 1-MeC tautomer with significant differences in C4-N4' and N1-C2 bond lengths (shorter in I), in N3-C4 and C2-N3 bond lengths (longer in I), as well as in ring angles at positions 2, 3, and 4. The effect of PtIV on the geometry of the cytosine ring is minimal and essentially restricted to the exocyclic imino group by slightly lengthening the C4-N4' bond. Formation of I occurs in 3 distinct steps, all of which were detected in soln., and the resp. species were isolated: (i) Pt coordination via N3, (ii) chelate formation through N3 and N4' with elimination of H2O from the complex, and (iii) addn. of H2O to the complex with reformation of Pt-OH and opening of the Pt-N3 bond. The acidity of the rare 1-MeC tautomer in its PtIV complexed form (deprotonation at N3) was detd. as .apprx.5.8 (pKa1) and .apprx.8.2 (pKa2).

IT 102149-63-3P

RL: PREP (Preparation)

(formation by intermol. condensation and subsequent intermol. condensation and hydrolysis of, methylcytosine linkage isomerization and tautomerization in relation to)

RN 102149-63-3 CAPLUS

CN Platinum(2+), (4-amino-1-methyl-2(1H)-pyrimidinonato-N3,N4)(4-amino-1methyl-2(1H)-pyrimidinone-N3)diamminehydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)

IT 101152-06-1

RL: RCT (Reactant)

(linkage isomerization, tautomerization via intermol. condensation and hydrolysis of)

RN 101152-06-1 CAPLUS

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)diamminedihydroxy-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

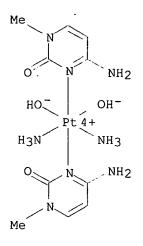
CM

CRN 101152-05-0

CMF C10 H22 N8 O4 Pt

CCI CCS

CDES 7:0C-6-12



CM 2

CRN 14797-55-8 CMF N 03

L22 ANSWER 38 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1986:417097 CAPLUS

DOCUMENT NUMBER:

105:17097

TITLE:

Unusual four-membered chelate rings of platinum(IV)

with a cytosine nucleobase

AUTHOR(S):

Schoellhorn, Helmut; Beyerle-Pfnuer, Rut; Thewalt,

Ulf; Lippert, Bernhard

CORPORATE SOURCE:

Anorg.-Chem. Inst., Tech. Univ. Muenchen, Garching,

8046, Fed. Rep. Ger.

SOURCE:

J. Am. Chem. Soc. (1986), 108(13), 3680-8

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Oxidn. of trans-[Pt(NH3)2(1-MeCH)2](NO3)2(1-MeCH = 1-methylcytosine,bound to Pt through N3) with H2O2 gives trans, trans, trans-[Pt(NH3)2(1-MeCH)2(OH)2](NO3)2.2H2O (I). From strongly acidic HNO3 soln. I crystallizes in its monoprotonated form trans, trans-[Pt(NH3)2(1-MeCH)2(OH)(OH2)](NO3)3.3H2O (II). In weakly to moderately acidic medium (HNO3) or on warming, I is converted into trans-[Pt(NH3)2(1-MeCH)(1-

Page 69

MeC) (OH] (NO3) 2.H2O (III) and trans, trans-[Pt(NH3) 2(1-MeC) 2] (NO3) 2.2H2O (IV), which contain 1 and 2 chelating, anionic 1-methylcytosinato ligands bound to the Pt through N3 and N4. The crystal structures of I, II, III, and IV were detd. The N3,N4 chelates in III and IV represent novel metal binding patterns with a cytosine nucleobase and at the same time the 1st examples of nucleobase chelates involving Pt. In these chelates, Pt-N3 and Pt-N4 distances are short and of comparable lengths, namely 1.969(13) and 2.032(16) .ANG. in II and 2.037(9) and 2.038(10) .ANG. in IV. The soln. behavior of I, II, III, and IV was studied by 1H NMR spectroscopy and potentiometric titrn. The pKa for the equil. II .dblharw. I + H+ is <1. Heating of I (II) in 3.5N HNO3 leads to displacement of 1-MeC. DCl (1N) causes substitution of OH ligands by Cl-, the substitution of the C5 proton of 1-MeC by Cl-, and eventually displacement of the modified nucleobase. Conversion of I into III and IV occurs in slight to moderate acidic soln. (pH 5.5-1.5). Isolated II (IV), when redissolved in H2O, equilibrates with I and IV (III). Two feasible ways of chelate formation are proposed, and the possible significance of 4-membered chelate rings in metal ions-nucleobase interactions is briefly discussed.

IT 102149-65-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

RN 102149-65-5 CAPLUS

CN Platinum(2+), (4-amino-1-methyl-2(1H)-pyrimidinonato-N3,N4)(4-amino-1methyl-2(1H)-pyrimidinone-N3)diamminehydroxy-, (OC-6-43)-, dinitrate, monohydrate (9CI) (CA INDEX NAME)

CM

CRN 102149-64-4 CMF C10 H20 N8 O3 Pt . 2 N O3

> 2 CM

CRN 102149-63-3 C10 H20 N8 O3 Pt CMF CCI CCS CDES 7:0C-6-43

CM 3

CRN 14797-55-8

N 03 CMF

IT 102210-45-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

102210-45-7 CAPLUS RN

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-N3)diamminedihydroxy-, dichloride, (OC-6-12)- (9CI) (CA INDEX NAME)

2 Cl-

ΙT 102149-59-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn., crystal structure and reaction with nitric acid) 102149-59-7 CAPLUS

RN

 ${\tt Platinum\,(2+)\,,\,\,bis\,(4-amino-1-methyl-2\,(1H)\,-pyrimidinone-N3)\,diamminedihydroxy-1}$ CN , (OC-6-12)-, dinitrate, dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 101152-06-1

C10 H22 N8 O4 Pt . 2 N O3 CMF

> 2 CM

CRN 101152-05-0

CMF C10 H22 N8 O4 Pt

CCI CCS

CDES 7:OC-6-12

CM 3

CRN 14797-55-8 CMF N O3

L22 ANSWER 39 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1987:648866 CAPLUS

DOCUMENT NUMBER:

107:248866

TITLE:

Complex compounds of platinum with chiral bioligands:

molecular structure and absolute configuration

AUTHOR(S):

Minacheva, L. Kh.; Slyudkin, O. P.; Porai-Koshits, M.

Α.

CORPORATE SOURCE:

USSR

SOURCE:

Probl. Sovrem. Bioneorgan. Khimii. Mater. Vyezd. Ses.,

Novosibirsk, 26-28 Marta, 1984, Novosibirsk (1986)

56-63

From: Ref. Zh., Khim. 1987, Abstr. No. 1B2143

DOCUMENT TYPE:

Journal Russian

LANGUAGE:

Title only translated.

AB Title only IT 38991-52-5

RL: PRP (Properties)

(mol. structure and abs. configuration of)

RN 38991-52-5 CAPLUS

H+

L22 ANSWER 40 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:140933 CAPLUS

DOCUMENT NUMBER: 104:140933

TITLE: A novel metal binding mode of cytosine nucleobases:

N(3), N(4) chelation

AUTHOR(S): Beyerle-Pfnuer, Rut; Schoellhorn, Helmut; Thewalt,

Ulf; Lippert, Bernhard

CORPORATE SOURCE: Anorg.-Chem. Inst., Tech. Univ. Muenchen, Garching,

D-8046, Fed. Rep. Ger.

SOURCE: J. Chem. Soc., Chem. Commun. (1985), (21), 1510-11

CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structure of [Pt(NH3)2L2](NO3)2.2H2O (I), prepd. from trans-[Pt(NH3)2(HL)2](NO3)2 (L = 1-methylcytosine) by oxidn. with H2O2 followed by warming in aq. HNO3, was detd. by x-ray crystallog. Crystals of I are monoclinic, space group P21/c, with a 7.230(3), b 10.576(4), c 13.186(2) .ANG., .beta. 100.92(3).degree., and d.(calcd.) = 2.138 g/cm3 for Z = 2. Results were refined to an R of 0.048 for 1419 reflections. I is the 1st example of anionic 1-methylcytosine acting as a chelating ligand through N-3 and N-4.

IT 101152-06-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and dehydroxylation of)

RN 101152-06-1 CAPLUS

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)diamminedihydroxy-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

CRN 101152-05-0

CMF C10 H22 N8 O4 Pt

CCI CCS

CDES 7:OC-6-12

2 CM

CRN 14797-55-8 CMF N 03

L22 ANSWER 41 OF 63 CAPLUS COPYRIGHT 2001 ACS

1986:60959 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 104:60959

TITLE: Cisplatin analogs. cis-Dichloro(amino

acid) (tert-butylamine) platinum (II) complexes and their

adducts with guanosine

Pasini, Alessandro; Bersanetti, Erik AUTHOR(S):

Dip. Chim. Inorg. Metallorg., Univ. Milan, Milan, CORPORATE SOURCE:

20133, Italy

Inorg. Chim. Acta (1985), 107(4), 259-67 SOURCE:

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal English LANGUAGE:

cis-[PtCl2(aaH)(tba)] (I) (aaH = NH2CHRCO2H {R = H, CH3 (L-, D-), CH(CH3)2 (L-, D-), CH2CH(CH3)2 (L-, D-), H2C6H5 (L-, D-), CH2OH (L-, D-), CHOHCH3 (L-, threo)}, proline (L-); tba = tert-BuNH2) were prepd. The CD spectra show that the phenylalanine and proline complexes have an anomalous conformation in water soln. Reaction of I with quanosine (quo) gave cis-[Pt(aaH)(tba)guo)2]Cl2 (II), in which IR and NMR evidence suggest N(7) coordination of guo. NMR and CD data suggest that in II the 2 guanosine ligands are arranged head-to-head and form a right-hand helix. bulkiness of the other ligands make rotation around the Pt-N(7) bonds a slow process on the NMR time scale. The chiroptical properties of II are not greatly affected by the abs. configuration of the amino acid, the right-hand screw probably arising by some guo-guo interaction since the derivs. of 9-methylguanine with chiral amino acids do not possess this conformation. Preliminary results on the reaction between I and calf thymus DNA are also briefly reported. They show that the interaction of I with DNA is of a lower extent than in the case of cisplatin and its

diamine analogs, and that it is independent on the configuration of the amino acids. All these results are briefly discussed and tentatively correlated with the low antitumor activity of I.

TΤ 99626-44-5

RL: PRP (Properties)

(reaction with guanosine and conformation of)

99626-44-5 CAPLUS RN

CN Platinate(1-), dichloro(2-methyl-2-propanamine)(L-prolinato-N1)-, hydrogen, (SP-4-3) - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
\text{C1}^- \\
 & \downarrow 2 + \\
\text{C1} - \text{Pt} & \text{NH}_2 - \text{Bu-t} \\
 & \downarrow \\
 & \downarrow$$

) н+

L22 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1985:124545 CAPLUS

DOCUMENT NUMBER:

102:124545

TITLE:

The reaction of platinum antitumor drugs with selected

nucleophiles. II. Preparation and characterization

of coordination compounds of platinum(II) and

L-histidine

AUTHOR(S):

Saudek, V.; Pivcova, H.; Noskova, D.; Drobnik, J.

CORPORATE SOURCE:

Inst. Macromol. Chem., Czech. Acad. Sci., Prague, 162

06, Czech.

SOURCE:

J. Inorg. Biochem. (1985), 23(1), 55-72

CODEN: JIBIDJ; ISSN: 0162-0134

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Various Pt(II)-L-histidine (HL) complexes were prepd. by reaction of K2PtCl4 (I) or cis-[Pt(NH3)2Cl2] (II) with HL and analyzed by 1H and 13C NMR spectroscopy, electrophoresis, and ion-exchange chromatog. HL may be coordinated to Pt by the imidazole imino group and/or the .alpha.-amino group; the carboxy group always remains free. I reacted with HL and HCl to give 2 isomers of cis-Pt(HL)2Cl2 in which HL is coordinated through the amino N or imino N atom. II reacts with HL to give a mixt. of compds. including cis-Pt(NH3)2HL (III) and 3 isomers of cis-[Pt(NH3)2(HL)2]Cl2, differing in the monodentate mode of coordination of HL. The reaction of III with HCl gave 2 isomers of Pt(NH3)(HL)Cl2 in which HL is ligated to Pt by an amino or imino group. The methods applied are suitable for analyzing reactions of HL with II under model conditions similar to physiol. conditions.

TΤ 95381-03-6P

RL: FORM (Formation, nonpreparative); PREP (Preparation)

(formation of, from platinum histidine complex and hydrochloric acid)

95381-03-6 CAPLUS RN

CN Platinate(1-), amminedichloro(L-histidinato-N3)-, hydrogen, monohydrochloride (9CI) (CA INDEX NAME)

HC1

● H+

L22 ANSWER 43 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1985:24580 CAPLUS

DOCUMENT NUMBER:

102:24580

TITLE:

cis-Diammineplatinum(IV) complexes of uracil through

chlorine treatment of a platinum(II) complex: oxidative addition to the metal and modification

(chlorine substitution, hypochlorous acid addition) of

the nucleobase

AUTHOR(S):

Mueller, Gerhard; Riede, Juergen; Beyerle-Pfnuer, Rut;

Lippert, Bernhard

CORPORATE SOURCE:

Anorg.-Chem. Inst., Tech. Univ. Muenchen, Garching,

III

8046, Fed. Rep. Ger.

SOURCE:

J. Am. Chem. Soc. (1984), 106(25), 7999-8001

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE:

LANGUAGE:

Journal English

OTHER SOURCE(S):

CASREACT 102:24580

GΙ

AB Reaction of cis-(NH3)2PtRCl (I; R = 1-methyluracil anion) with Cl2 in aq. soln. gave 3 Pt(IV)-uracil derivs. II (R = H, Cl) and III, depending on reaction conditions. In formation of II (R = H) from I and chlorine water, the expected oxidn. of Pt(II) to Pt(IV) took place. Treating of I with Cl gas gave II (R = Cl) in which the H at the C(5) position of the heterocyclic ring was replaced by Cl. In formation of III, from I and Cl in low yield, or from II (R = Cl) and Cl in good yield, HOCl added to the double bond of the uracil ligand. The x-ray crystal structures of II (R = Cl) and III, which were similar, showed exocyclic O atoms were locked between a pair of Cl ligands and one Cl and one NH3 ligand, resp., leading

to small dihedral angles between the rings and the Pt(NH3)2ClN(3) plane.

IT 93474-05-6P 93474-06-7P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

RN 93474-05-6 CAPLUS

CN Platinum, diamminetrichloro(5-chloro-1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-31)- (9CI) (CA INDEX NAME)

RN 93474-06-7 CAPLUS

CN Platinum, diamminetrichloro(5,5-dichlorodihydro-6-hydroxy-1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-31)- (9CI) (CA INDEX NAME)

IT 93474-04-5P

RN 93474-04-5 CAPLUS

CN Platinum, diamminetrichloro(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-31)- (9CI) (CA INDEX NAME)

L22 ANSWER 44 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1983:498147 CAPLUS

DOCUMENT NUMBER:

99:98147

TITLE:

Mononuclear complexes of cis-diammineplatinum(II) and

-(IV) with .alpha.-pyridone. Structures of

cis-[Pt(NH3)2(C5H4NOH)2]Cl2, mer-[Pt(NH3)2(C5H4NO)Cl3], and cis-

[Pt(NH3)2(C5H4NOH)C1](NO3)

AUTHOR(S):

SOURCE:

Hollis, L. Steven; Lippard, Stephen J.

CORPORATE SOURCE:

Dep. Chem., Columbia Univ., New York, NY, 10027, USA

Inorg. Chem. (1983), 22(19), 2708-13

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE:

Journal English

LANGUAGE:

cis-[Pt(NH3)2(HL)2]Cl2 (I), mer-[Pt(NH3)2LCl3] (II), and cis-[Pt(NH3)2(HL)Cl]NO3 (III) (HL = .alpha.-pyridone) were prepd. and characterized by x-ray diffraction. The 2-hydroxypyridine ligands in I are oriented in the anti rotational conformation, and the resulting atropisomer has crystallog. required C2 symmetry. The isolation and characterization of these mononuclear complexes contribute significantly to the anal. of the reaction chem. of cis-diammineplatinum(II) with .alpha.-pyridone that leads to the formation of the cis-diammineplatinum .alpha.-pyridone blue. Crystallog. data are as follows: I is monoclinic, a 9.072(2), b 22.875(3), c 8.003(1) .ANG., .beta. 109.24(1).degree., V = 1568 .ANG.3, Z = 4, space group C2/c; II is monoclinic, a 7.490(2), b 9.309(2), c 15.294(3) .ANG., .beta. 100.09(3).degree., V = 1050 .ANG.3, Z = 4, space group P21/c; III is triclinic, a 10.706(3), b 12.552(4), c 4.151(1) .ANG., .alpha. 95.57(1), .beta. 92.32(3), .gamma.

99.05(3).degree., V = 547.4 .ANG.3, Z = 2, space group P.hivin.1.

IT 86471-90-1P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

RN 86471-90-1 CAPLUS

CN Platinum, diamminetrichloro(2(1H)-pyridinonato-N1)-, (OC-6-31)- (9CI) (CA INDEX NAME)

L22 ANSWER 45 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1982:448429 CAPLUS

DOCUMENT NUMBER: 97:48429

TITLE: ESR study on complexes formed on reaction of

cis-dichlorodiammineplatinum(II) with cytosine and

cytidine

AUTHOR(S): Neubacher, H.; Krieger, J.; Zaplatynski, P.; Lohmann,

W.

CORPORATE SOURCE: Inst. Biophys., Justus-Liebig-Univ., Giessen, D-6300,

Fed. Rep. Ger.

SOURCE: Z. Naturforsch., B: Anorg. Chem., Org. Chem. (1982),

37B(6), 790-2

CODEN: ZNBAD2; ISSN: 0340-5087

DOCUMENT TYPE: Journal LANGUAGE: English

AB The ESR spectra of novel paramagnetic complexes between cis-dichlorodiammineplatinum(II) and cytosine or cytidine in aq. solns. are presented and discussed. The results imply a complex contg. a bipuglear motal motal bonded Bt majety with an unpaired electron spin

binuclear metal-metal bonded Pt moiety with an unpaired electron spin

delocalized over the dz2-orbitals.

IT 82383-99-1 82384-00-7

RL: PRP (Properties)

(ESR of)

RN 82383-99-1 CAPLUS

CN Platinum, bis(4-amino-2(1H)-pyrimidinone-N3)tetraamminetetrachlorodi-, (Pt-Pt), stereoisomer (9CI) (CA INDEX NAME)

Page 79

RN 82384-00-7 CAPLUS

CN Platinum, tetraamminetetrachlorobis(cytidine-N3)di-, (Pt-Pt), stereoisomer (9CI) (CA INDEX NAME)

L22 ANSWER 46 OF 63 CAPLUS COPYRIGHT 2001 ACS

1981:149402 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 94:149402

Crystal structures of trans-dichloroammine(1-TITLE:

methylcytosine-N3) platinum (II) hemihydrate,

[PtCl2(NH3)(C5H7N3)].1/2H2O, and trans-diamminebis(1methylcytosine-N3)platinum(II) dinitrate. Evidence

for the unexpected lability of ammonia in a

cis-diammineplatinum(II) complex

Lippert, B.; Lock, C. J. L.; Speranzini, R. A. AUTHOR(S):

CORPORATE SOURCE: Inst. Mater. Res., McMaster Univ., Hamilton, ON, L8S

4M1, Can.

SOURCE: Inorg. Chem. (1981), 20(3), 808-13

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE: Journal LANGUAGE: English

Two trans-ligand Pt(II) complexes were isolated and studied. AB trans-PtCl2(NH3)L.0.5H20 (I) (L = 1-methylcytosine-N3) has the space group C2/c with a 14.697(6), b 6.816(1), c 23.225(4) .ANG., .beta. 112.03(2).degree., and Z = 8. trans-[Pt(NH3)2L](NO3)2 (II) has space group P21/c with a 6.834(2), b 10.315(2), c 13.349(3) .ANG., .beta. 107.90(2).degree., and Z = 2. Data for both compds. were collected with use of Mo K.alpha. radiation and a Syntex P21 diffractometer. Both crystal structures were detd. by std. methods. I was refined to R1 = 0.0612 and R2 = 0.0775 on the basis of 2503 independent reflections. final R1 = 0.0346 and R2 = 0.0410 for II were based on 1687 independent reflections. I has normal bond distances [Pt-Cl = 2.288(5), 2.296(5)].ANG.; Pt-N(pyrimidine) = 2.03(1) .ANG.; Pt-N(ammonia) = 2.04(1) .ANG.] and angles, and the pyrimidine ring is at an angle of 64.degree. to the ligand square plane. I is formed from cis-[Pt(NH3)2ClL]Cl in aq. soln. at room temp. A mechanism is proposed for its formation, and possible implications with regard to the binding properties of cis-Pt(NH3)2Cl2 are

discussed. II also has normal bond distances [Pt-N(ammonia) = 2.067(10 .ANG.; Pt-N(pyrimidine) = 2.023(8) .ANG.] and angles; the pyrimidine-square-plane dihedral angle is larger (78.degree.).

TΤ 76068-65-0P

> RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

76068-65-0 CAPLUS RN

Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-N3)amminedichloro-, hydrate CN (2:1), (SP-4-1)- (9CI) (CA INDEX NAME)

●1/2 H₂O

L22 ANSWER 47 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1981:472299 CAPLUS

DOCUMENT NUMBER:

95:72299

TITLE:

Study of the thermal stability of [Pt(NH3)2LC1]C1

complexes

AUTHOR(S):

Kukushkin, Yu. N.; Andronov, E. A.; Postnikova, E. S.;

Lukicheva, T. M.; Krylova, G. S.

CORPORATE SOURCE:

Leningr. Tekhnol. Inst., Leningrad, USSR

SOURCE:

Zh. Prikl. Khim. (Leningrad) (1981), 54(2), 239-42

CODEN: ZPKHAB; ISSN: 0044-4618

DOCUMENT TYPE:

Journal LANGUAGE: Russian

AB cis-[Pt(NH3)2LCl]Cl [L = Et2SO, Pr2SO, tetramethylene sulfoxide, (PhCH2)2SO, thioxane, thiophane] were prepd. by the reaction of cis- or trans-[PtL2Cl2] in CHCl3 or Me2CO with NH3 gas. cis-[Pt(NH3)2LCl]Cl thermally decomp. to [Pt(NH3)LC12] with loss of NH3; and for L = thiophane and tetramethylene sulfoxide to [Pt2(NH3)]4LC12]C12 and for L = Et2SO, Pr2SO, (PhCH2)2SO, and thioxane to [Pt(NH3)3Cl]Cl with the loss of L.

IT 77689-88-4P 77701-60-1P 77716-73-5P

RL: FORM (Formation, nonpreparative); PREP (Preparation) (formation of, in thermolysis reaction)

RN77689-88-4 CAPLUS

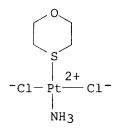
CN Platinum, amminedichloro(tetrahydrothiophene 1-oxide-S1)- (9CI) (CA INDEX NAME)

RN 77701-60-1 CAPLUS

CN Platinum, amminedichloro(tetrahydrothiophene) - (9CI) (CA INDEX NAME)

RN 77716-73-5 CAPLUS

CN Platinum, amminedichloro(1,4-oxathiane-S4)- (9CI) (CA INDEX NAME)



L22 ANSWER 48 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1982:35500 CAPLUS

DOCUMENT NUMBER: 96:35500

TITLE: Tris(nucleobase) complexes derived from

cis-diammineplatinum(II) chloride

AUTHOR(S): Lippert, Bernhard

CORPORATE SOURCE: Anorg.-Chem. Inst., Tech. Univ., Garching, D-8046,

Fed. Rep. Ger.

SOURCE: Inorg. Chim. Acta (1981), 56(2), L23-L24

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal LANGUAGE: English

AB [Pt(NH3)C3](ClO4)2 (C = 1-methylcytosine) was prepd. by sequential treatment of trans-Pt(NH3)CCl2 with AgClO4 and C. Analogously obtained

was trans-[Pt(NH3)CG2](ClO4)2 (G = 9-ethylguanine).

IT 80103-36-2

RL: RCT (Reactant)

(sequential reaction of, with silver perchlorate and 1-methylcytosine)

RN 80103-36-2 CAPLUS

CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-N3)amminedichloro-, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 ANSWER 49 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1980:578637 CAPLUS

DOCUMENT NUMBER:

93:178637

TITLE:

Study of the circular dichroism of diastereomers of trans-monoamminemonoprolinedichloroplatinum. Crystal

structure and absolute configuration of

trans-[Pt{L-(RN)ProH}(NH3)Cl2]

AUTHOR(S):

Slyudkin, O. P.; Minacheva, L. Kh.; Kerzhentsev, M. A.; Sadikov, G. G.; Antsyshkina, A. S.; Porai-Koshits,

M. A.

Journal

CORPORATE SOURCE:

Inst. Obshch. Neorg. Khim. im. Kurnakova, Moscow, USSR

SOURCE: Koord. Khim. (1980), 6(7), 1097-103

CODEN: KOKHDC

DOCUMENT TYPE:

LANGUAGE: Russian

AB trans-[Pt{(RN)ProH}(NH3)Cl2] (I) and trans-[Pt{(SN)ProH}(NH3)Cl2] (ProH = L-proline) were prepd. and characterized by CD, electronic, and IR spectra. I is orthorhombic, space group P21221, with a 6.724(3), b 12.621(4), c 12.641(5) .ANG.; Z = 4, d.(calcd.) = 2.28. The abs. configurations of the asym. N and C atoms are R and S, resp., in I.

IT 75109-78-3P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and CD of)

RN 75109-78-3 CAPLUS

H+

IT 75109-77-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn., crystal structure and CD of)

RN 75109-77-2 CAPLUS

CN Platinate(1-), amminedichloro(L-prolinato-N1)-, hydrogen,

[SP-4-1-(trans)]- (9CI) (CA INDEX NAME)

H +

L22 ANSWER 50 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1974:89026 CAPLUS

DOCUMENT NUMBER: 80:89026

TITLE: Optical activity of mixed platinum(II) proline-glycine

complexes

AUTHOR(S): Slyudkin, O. P.; Adrianova, O. N.; Volshtein, L. M.

CORPORATE SOURCE: Inst. Obshch. Neorg. Khim. im. Kurnakova, Moscow, USSR

SOURCE: Zh. Neorg. Khim. (1973), 18(11), 3028-32

CODEN: ZNOKAQ

DOCUMENT TYPE: Journal LANGUAGE: Russian

The ORD, CD, and absorption spectra of several mixed Pt(II) proline (PrOH)-glycine (GlyH) bis-chelates of the trans configuration, e.g., ([Pt(L-Pro)(Gly)], [Pt(L-Pro)(Gly)(NH3)2], [Pt(L-PrOH)(GlyH)(NH3)2]Cl2, [Pt(L-PrOH)(GlyH)Cl2], and [Pt(L-Pro)(GlyH)Cl]), were studied at 250-600 nm in order to find out, whether the stereochem. relations for the N-atom of the mono- and bidentate L-proline remain the same as those found for the monoproline compds. In these bis-chelates L-proline is coordinated stereospecifically with the formation of S-configuration on the N-atom. Racemization of this configuration proceeds via opening of the Pt-O bond. The [Pt(L-Pro)(Gly).HCl] complex contains a bidentate proline and a monodentate glycine: [Pt(L-Pro)(GlyH)Cl].

IT 38991-52-5

RL: PRP (Properties)

(optical activity of)

RN 38991-52-5 CAPLUS

CN Platinate(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 ANSWER 51 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1974:33371 CAPLUS

DOCUMENT NUMBER:

80:33371

TITLE:

AB

Optical activity of platinum(II) complexes with mono-

and bidentate L-proline

AUTHOR(S):

Slyudkin, O. P.; Adrianova, O. N.; Chel'stov, P. A.;

Volshtein, L. M.

CORPORATE SOURCE: SOURCE:

Inst. Obshch. Neorg. Khim., Moscow, USSR
Zh. Neorg. Khim. (1973), 18(10), 2631-5

CODEN: ZNOKAQ

DOCUMENT TYPE:

Journal Russian

LANGUAGE:

The absorption, CD, and ORD spectra of [PtL(NH3)-C1] (HL = L-proline), [Pt(HL)NH3C12], K[PtLC12], and K[Pt-(HL)C13], and [PtL(NH3)3]C1 indicate that, in contrast to bidentate HL, monodentate L- is nonstereospecifically coordinated to N. The opening of the Pt-L-proline chelate cycle is

accompanied by racemization of an asym. N donor atom.

IT 38991-52-5

RL: RCT (Reactant)

(stereochem. of, spectra in relation to)

RN 38991-52-5 CAPLUS

CN Platinate(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)- (9CI) (CA INDEX NAME)

H+

L22 ANSWER 52 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1973:89212 CAPLUS

DOCUMENT NUMBER:

78:89212

TITLE:

Stability of platinum(II) complexes with secondary

heterocyclic amines

AUTHOR(S):

Kukushkin, Yu. N.; Yurinov, V. A.

CORPORATE SOURCE:

USSR

SOURCE:

Zh. Neorg. Khim. (1973), 18(1), 182-8

CODEN: ZNOKAQ

DOCUMENT TYPE:

Journal

LANGUAGE:

Russian

AB The instability consts. are given for a series of Pt(II) and Pt(IV) complexes with heterocyclic amines. Fifteen Pt-piperidine (I) and 4 Pt-morpholine (II) complexes were prepd., the latter being more stable than the piperidine complexes. The exptl. stability consts. were compared with the published results. For Pt(IV), the stability of the type-[PtL4Cl2] complexes increases with L in the order Cl < py < EtNH2 < piperidine .apprxeq. NH3 < MeNH2 and of the type [PtX6] complexes with X in the order Cl < Br < piperidine < CN. The stability of the [PtIIL4]

increases with L in the order Cl < Br < I < py < NH3 < EtNH2 < piperidine < morpholine < MeNH2 < CN < en.

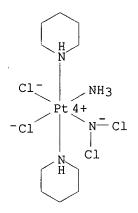
IT 41476-53-3P 41476-54-4P 41518-02-9P

41518-03-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of) 41476-53-3 CAPLUS

RN 41476-53-3 CAPLUS
CN Platinum(1+), amminedichlorodichloramidobis(piperidine)-, chloride, (OC-6-14)- (9CI) (CA INDEX NAME)



Cl-

RN 41476-54-4 CAPLUS

CN Platinum(2+), diamminedichlorobis(piperidine)-, dichloride, (OC-6-13)-(9CI) (CA INDEX NAME)

2 Cl⁻

RN 41518-02-9 CAPLUS

CN Platinum(2+), diamminedichlorobis(piperidine)-, dichloride, (OC-6-32)-(9CI) (CA INDEX NAME)

2 Cl-

RN 41518-03-0 CAPLUS CN Platinum(1+), amminedichlorodichloramidobis(piperidine)-, chloride (9CI) (CA INDEX NAME)

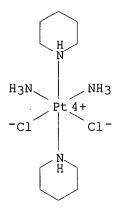
Cl-

ΙT 41476-65-7

> RL: PRP (Properties) (stability of)

RN 41476-65-7 CAPLUS

Platinum(2+), diamminedichlorobis(piperidine)-, (QC-6-32)- (9CI) CN INDEX NAME)



L22 ANSWER 53 OF 63 CAPLUS COPYRIGHT 2001 ACS

1973:520052 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 79:120052

Infrared spectra and structure of L-proline-TITLE:

platinum(II) complexes

Slyudkin, O. P.; Selitskaya, N. D.; Volshtein, L. M. AUTHOR(S):

Novosib. Gos. Univ., Novosibirsk, USSR CORPORATE SOURCE:

Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk SOURCE:

(1973), (4), 44-8

CODEN: IZSKAB

DOCUMENT TYPE: Journal LANGUAGE: Russian

The ir spectra (400-4000 cm-1) were studied of 15 monoproline, diproline, and proline-glycine Pt(II) complexes. The empirical assignment of some characteristic bands is given. The data confirm the structure of the

complexes predicted by V. and S. (1972) from chem. studies.

ΙT 38991-52-5

RL: PRP (Properties)

(ir spectrum and structure of)

RN 38991-52-5 CAPLUS

Platinate(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)-. CN (9CI) (CA INDEX NAME)

 H^+

L22 ANSWER 54 OF 63 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1972:559606 CAPLUS

DOCUMENT NUMBER: 77:159606

TITLE: Platinum(II) diproline compounds

Page 88

AUTHOR(S):

Volshtein, L. M.; Slyudkin, O. P.

CORPORATE SOURCE: SOURCE:

Novosib. Gos. Univ., Novosibirsk, USSR Zh. Neorg. Khim. (1972), 17(8), 2239-44

CODEN: ZNOKAQ

DOCUMENT TYPE:

Journal

LANGUAGE: Russian

AB The reaction of K[PtLCl2] with excess HL (HL = L-proline) gave

trans-[PtL(LH)Cl] and cis-PtL2. The prolonged treatment of

trans-[PtL(LH)Cl] with warm KOH gave trans-PtL2. PtL2(thio)2 (thio =

thiourea), PtL2(NH3)2, and Pt(LH)NH3Cl2 were prepd. also.

ΙT 38991-52-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

38991-52-5 CAPLUS RN

CN Platinate(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)-(9CI) (CA INDEX NAME)

H+

L22 ANSWER 55 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1970:38390 CAPLUS

DOCUMENT NUMBER:

72:38390

TITLE:

Complexes of platinum with morpholine

AUTHOR(S):

Kukushkin, Yu. N.; Yurinov, V. A.

CORPORATE SOURCE:

USSR

SOURCE:

Zh. Neorg. Khim. (1969), 14(11), 3049-52

CODEN: ZNOKAQ

DOCUMENT TYPE:

LANGUAGE:

Journal Russian

AB The following new complexes of morpholine (L) with Pt(II) or Pt(IV) were prepd.: cis-[PtL2Cl2], cis-[PtL2Cl4], cis-[PtL2Cl3OH], trans- and cis-[Pt(NH3)2L2]Cl2, trans- and cis-[Pt(NH3)2L2Cl2]C 12, trans- and cis-[PtNCl2(NH3)L2-Cl2]Cl. L is easily replaced by H2O, more so in Pt(IV) complexes. Instability consts. of trans- and cis-[Pt(NH3)2L2]Cl2 are 1.2 .times. 10-10 and 1.1 .times. 10-13, resp.

ĬΤ 25145-68-0P 25145-69-1P 25145-70-4P

25246-34-8P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

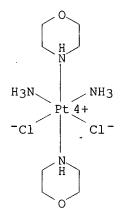
25145-68-0 CAPLUS RN

CN Platinum(2+), diamminedichlorobis(morpholine)-, dichloride, trans- (8CI) (CA INDEX NAME)

2 Cl-

RN 25145-69-1 CAPLUS

CN Platinum(2+), diamminedichlorobis(morpholine)-, dichloride, cis- (8CI) (CA INDEX NAME)



2 Cl-

RN 25145-70-4 CAPLUS

CN Platinum(1+), amminedichloro(dichloramido)bis(morpholine)-, chloride,
 trans- (8CI) (CA INDEX NAME)

● C1-

RN 25246-34-8 CAPLUS

CN Platinum(1+), amminedichloro(dichloramido)bis(morpholine)-, chloride, cis-(8CI) (CA INDEX NAME)

C1-

L22 ANSWER 56 OF 63 USPATFULL

ACCESSION NUMBER:

93:76537 USPATFULL

TITLE:

Pt(IV) complexes as anti-tumor agents

INVENTOR(S):

Abrams, Michael J., Glenmore, PA, United States Giandomenico, Christen M., Exton, PA, United States

Murrer, Barry A., Reading, United Kingdom Vollano, Jean F., Exton, PA, United States

PATENT ASSIGNEE(S):

Johnson Matthey, Inc., Valley Forge, PA, United States

(U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5244919 19930914 APPLICATION INFO.: US 1991-723971 19910701 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 1990-602931, filed on 25 Oct 1990, now patented, Pat. No. US 5072011 which is a

continuation-in-part of Ser. No. US 1988-151674, filed

on 2 Feb 1988, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Lewis, Michael
ASSISTANT EXAMINER: Hendricks, Stuart L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman

NUMBER OF CLAIMS: 2 EXEMPLARY CLAIM: 1 LINE COUNT: 841

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A Pt(IV) complex of the formula ##STR1## wherein A and A' are NH.sub.3 or an amino group; R and R.sup.1 are hydrogen, alkyl, alkenyl, aryl, aralkyl, alkylamino or alkoxy or functionalized derivatives thereof; and X is halogen or alkyl mono- or dicarboxylate. The complexes have high antitumor activity, particularly when administered orally.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 129598-45-4P

(prepn. of, as antitumor agent)

RN 129598-45-4 USPATFULL

CN Platinum, bis(acetato-0)amminedichloro(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)

L22 ANSWER 57 OF 63 USPATFULL

ACCESSION NUMBER: 93:20740 USPATFULL
TITLE: Trans-Pt (IV) compounds

INVENTOR(S): Barnard, Christopher F. J., Reading, United Kingdom
PATENT ASSIGNEE(S): Johnson Matthey Public Limited Company, London, England

(non-U.S. corporation)

PATENT INFORMATION: US 5194645 19930316

APPLICATION INFO.: US 1992-848681 19920309 (7)

NUMBER DATE

PRIORITY INFORMATION: GB 1991-5037 19910309
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER:

Prescott, Arthur C.

LEGAL REPRESENTATIVE:

Cushman, Darby & Cushman

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

14 1

LINE COUNT:

741

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Trans-Pt(IV) compounds of general formula

[PtX.sub.2 Y.sub.2 L.sup.1 L.sup.2)]

where X is halogen, Y is halogen, hydroxyl or carboxylate and each L is an amine ligand, providing L.sup.1 and L.sup.2 are not both NH.sub.3 are surprisingly active against cancer cells, in contrast to expectations that all trans-Pt compounds are inactive.

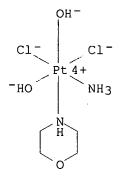
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 146924-17-6P

(prepn. of, as antitumor pharmaceutical)

RN 146924-17-6 USPATFULL

Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-12)- (9CI) CN INDEX NAME)



L22 ANSWER 58 OF 63 USPATFULL

ACCESSION NUMBER:

91:100525 USPATFULL

TITLE: INVENTOR(S):

Pt(IV) complexes Abrams, Michael J., Glenmore, PA, United States

Giandomenico, Christen, Exton, PA, United States Murrer, Barry A., Reading, Great Britain

Vollano, Jean F., Exton, PA, United States

PATENT ASSIGNEE(S):

Johnson Matthey, Inc., Valley Forge, PA, United States

DATE

(U.S. corporation)

PATENT INFORMATION: US 5072011 19911210 US 1990-602931 APPLICATION INFO.: 19901025 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1989-296776, filed on 13 Jan 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-151674, filed on 2 Feb 1988, now

NUMBER KIND

abandoned

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Straub, Gary P.

ASSISTANT EXAMINER: LEGAL REPRESENTATIVE:

Hendrickson, Stuart L. Cushman, Darby & Cushman

Searched by Barb O'Bryen, STIC 308-4291

NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 860

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A Pt(IV) complex of the formula ##STR1## wherein A and A' are NH.sub.3 or an amino group; R and R' are hydrogen, alkyl, alkenyl, aryl, aralkyl, alkylamino or alkoxy or functionalized derivatives thereof; and X is halogen or alkyl mono- or dicarboxylate. The complexes have high antitumor activity, particularly when administered orally.

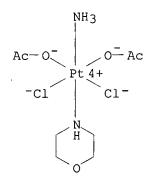
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 129598-45-4P

(prepn. of, as antitumor agent)

RN 129598-45-4 USPATFULL

CN Platinum, bis(acetato-O)amminedichloro(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)



L22 ANSWER 59 OF 63 USPATFULL

ACCESSION NUMBER: 91:50465 USPATFULL

TITLE: Platinum complexes with one radiosensitizing ligand

INVENTOR(S): Skov, Kirsten A., Vancouver, Canada

Farrell, Nicholas P., Winooski, VT, United States

Chaplin, David J., Richmond, Canada

PATENT ASSIGNEE(S): The British Columbia Cancer Foundation, Vancouver,

Canada (non-U.S. corporation)

NUMBER KIND DATE US 5026694 PATENT INFORMATION: 19910625 APPLICATION INFO.: US 1989-374356 19890630 (7) Continuation-in-part of Ser. No. US 1987-37498, filed RELATED APPLN. INFO.: on 13 Apr 1987, now patented, Pat. No. US 4921963 DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Friedman, Stanley J. ASSISTANT EXAMINER: Hollinden, Gary E. Irell & Manella LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 30 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 1001

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods to inhibit tumor growth and to radiosensitize hypoxic cells and pharmaceutical compositions therefor are disclosed. These methods and compositions use compounds of the formula

PtX.sub.n (NR.sub.2 H) (L)

(1)

wherein n is 1 or 2, and

wherein when n is 2, X is a monovalent biologically acceptable anion, and when n is 1, X is a divalent biologically acceptable anion;

each R is independently H or alkyl, or both Rs together are a piperidino or morpholino residue; and

L is a radiosensitizing ligand selected from a mononitro-substituted imidazole, a mononitro-substituted pyrazole, a mononitro-substituted thiazole and a mononitro-substituted isothiazole.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 110302-83-5 110321-22-7 112198-62-6

114532-23-9 121281-51-4 121350-02-5

121350-03-6 121350-04-7 121350-05-8

121350-06-9 121350-07-0 121668-91-5

121668-92-6 121703-32-0 121703-33-1

(as radiosensitizer, for neoplasm treatment)

RN 110302-83-5 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 110321-22-7 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 112198-62-6 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114532-23-9 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121281-51-4 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121350-02-5 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]- (9CI) (CA INDEX NAME)

RN 121350-03-6 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)(9CI) (CA INDEX NAME)

RN 121350-04-7 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]- (9CI) (CA INDEX NAME)

RN 121350-05-8 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)- (9CI) (CA INDEX NAME)

RN 121350-06-9 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121350-07-0 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121668-91-5 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)- (9CI) (CA INDEX NAME)

RN 121668-92-6 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)- (9CI) (CA INDEX NAME)

RN 121703-32-0 USPATFULL

RN 121703-33-1 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 ANSWER 60 OF 63 USPATFULL

ACCESSION NUMBER:

90:71847 USPATFULL

TITLE:

Monoclonal antibody - platinum co-ordination compound

complex

INVENTOR(S):

Heffernan, James G., Pangbourne, England

Hydes, Paul C., Reading, England

Picker, Donald H., Narbert, PA, United States

PATENT ASSIGNEE(S):

Johnson Matthey PLC, London, England (non-U.S.

corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4956454		19900911
APPLICATION INFO.:	US 1988-184140		19880421 (7)
RELATED APPLN. INFO.:	Division of Ser.	No. US	1986-873130, fi.

RELATED APPLN. INFO.: Division of Ser. No. US 1986-873130, filed on 11 Jun 1986, now patented, Pat. No. US 4760155 which is a continuation-in-part of Ser. No. US 1984-625251, filed

on 27 Jun 1984, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION: DOCUMENT TYPE:	EP 1985-304131 Utility	19850611
FILE SEGMENT: PRIMARY EXAMINER:	Granted Draper, Garnette	
LEGAL REPRESENTATIVE: NUMBER OF CLAIMS:	Cushman, Darby &	Cushman

NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1

LINE COUNT: 455

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Platinum co-ordination compounds comprising at least one amine ligand and a functional group remotely bonded to the amine ligand, which functional group may be linkable to a monoclonal antibody to provide a moiety which stabilizes the antibody against in vivo hydrolysis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 103436-53-9P

(prepn. and reaction of, with silver nitrate and hydrochloric acid)

RN 103436-53-9 USPATFULL

CN Platinum, amminediiodo(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

IT 103436-43-7P 103436-44-8P

(prepn. of, for linking to monoclonal antibodies, for drug delivery)

RN 103436-43-7 USPATFULL

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 103436-44-8 USPATFULL

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)

L22 ANSWER 61 OF 63 USPATFULL

ACCESSION NUMBER: 90:34216 USPATFULL

(7)

Page 100

TITLE:

Platinum complexes with one radiosensitizing ligand

INVENTOR(S):

Skov, Kirsten A., Vancouver, Canada Farrell, Nicholas P., Winooski, VT, United States

Chaplin, David J., Richmond, Canada

PATENT ASSIGNEE(S):

British Columbia Cancer Foundation, Vancouver, Canada

(non-U.S. corporation)

NUMBER. KIND DATE -----

PATENT INFORMATION: APPLICATION INFO.:

US 4921963 19900501 US 1987-37498 19870413

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Lieberman, Paul McNally, John F. Irell & Manella

LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: EXEMPLARY CLAIM:

ASSISTANT EXAMINER:

13 1

NUMBER OF DRAWINGS:

4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT:

807 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

Complexes of platinum II containing a single radiosensitizer ligand and an amino or ammine substituent shows superior binding to DNA and are useful in chemotherapy and sensitization of hypoxic tumors to radiation. The chemotherapeutic value of these compounds is enhanced by administration of vasoactive agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 110302-83-5 110321-22-7 112198-62-6

114532-23-9 121281-51-4 121350-02-5

121350-03-6 121350-04-7 121350-05-8

121350-06-9 121350-07-0 121668-91-5

121668-92-6 121703-32-0 121703-33-1

(as radiosensitizer, for neoplasm treatment)

RN 110302-83-5 USPATFULL

Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA CN INDEX NAME)

RN 110321-22-7 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)-(9CI) (CA INDEX NAME)

RN 112198-62-6 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 114532-23-9 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121281-51-4 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

09/678595

RN 121350-02-5 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1acetamide-N3]- (9CI) (CA INDEX NAME)

RN 121350-03-6 USPATFULL

Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-CN (9CI) (CA INDEX NAME)

121350-04-7 USPATFULL RN

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1ethanol-N3]- (9CI) (CA INDEX NAME)

RN 121350-05-8 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)- (9CI) (CA INDEX NAME)

RN 121350-06-9 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121350-07-0 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121668-91-5 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)- (9CI) (CA INDEX NAME)

RN 121668-92-6 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)- (9CI) (CA INDEX NAME)

RN 121703-32-0 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)

RN 121703-33-1 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)

L22 ANSWER 62 OF 63 USPATFULL

ACCESSION NUMBER:

90:13532 USPATFULL

TITLE:

Ammine-alicyclic amine-platinum complexes and antitumor

agents

INVENTOR(S):
Totani, Tetsushi, Hyogo, Japan

Aono, Katsutoshi, Nara, Japan Adachi, Yasuko, Osaka, Japan

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Fukushima, Japan (non-U.S.

corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 4902797 19900220

APPLICATION INFO.: US 1987-135061 19871218 (7)

NUMBER DATE

PRIORITY INFORMATION: JP 1986-303529 19861218

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Berch, Mark L.

NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1,2
LINE COUNT: 622

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of the formula (I): ##STR1## (wherein R is C.sub.1 -C.sub.6 alkyl, hydroxy, carboxy, C.sub.1 -C.sub.6 alkoxy, halogen or oxo; m is an integer from 2 to 7; X and Y each is chlorine or nit-rato ligand, or taken together form --OCOCH(R.sup.1)O--, OCOCOO--, ##STR2## R.sup.1 is hydrogen, C.sub.1 -C.sub.5 alkyl, hydroxymethyl, halogmethyl or phenyl; R.sup.2 is hydrogen or C.sub.1 -C.sub.5 alkyl; and n is an integer from 2 to 5), being useful as antitumor agents is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 116219-17-1P 116219-18-2P 116219-19-3P

116219-20-6P 116219-21-7P 116219-22-8P

116219-23-9P 116219-24-0P 116219-25-1P

116219-26-2P 116219-27-3P 116219-28-4P

116219-29-5P 116219-30-8P 116219-31-9P

116235-96-2P 116297-79-1P 116297-80-4P

(prepn. of, as antitumor agent)

RN 116219-17-1 USPATFULL

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-18-2 USPATFULL

CN Platinum, amminebis(nitrato-O)(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-19-3 USPATFULL

CN Platinum, ammine[ethylpropanedioato(1-)-0,0'](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-20-6 USPATFULL

CN Platinum, ammine[ethanedioato(2-)-0,0'](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-21-7 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2](pyrrolidine)-, (SP-4-4)- (9CI) (CA INDEX NAME)

RN 116219-22-8 USPATFULL

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-23-9 USPATFULL

CN Platinum, amminebis(nitrato-0)(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-24-0 USPATFULL

CN Platinum, ammine[ethylpropanedioato(2-)-0,0'](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-25-1 USPATFULL

CN Platinum, ammine[ethanedioato(2-)-0,0'](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-26-2 USPATFULL

CN Platinum, amminedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-27-3 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2](piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-28-4 USPATFULL

CN Platinum, amminedichloro(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-29-5 USPATFULL

CN Platinum, amminebis(nitrato-O)(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-30-8 USPATFULL

CN Platinum, amminedichloro(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-31-9 USPATFULL

CN Platinum, amminebis(nitrato-O)(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-96-2 USPATFULL

CN Platinum, amminedichloro(pyrrolidinė)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116297-79-1 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116297-80-4 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2](piperidine)-, (SP-4-4)- (9CI) (CA INDEX NAME)

IT 116219-32-0P 116219-33-1P 116235-97-3P

116235-98-4P

(prepn. of, as antitumor agent intermediate)

RN 116219-32-0 USPATFULL

CN Platinum, amminediiodo(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116219-33-1 USPATFULL

CN Platinum, amminediiodo(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-97-3 USPATFULL

CN Platinum, amminediiodo(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 116235-98-4 USPATFULL

CN Platinum, amminechloroiodo(3-pyrrolidinol-N1)- (9CI) (CA INDEX NAME)

L22 ANSWER 63 OF 63 USPATFULL

ACCESSION NUMBER: 88:47362 USPATFULL

TITLE: Platinum co-ordination compounds

INVENTOR(S): Heffernan, James G., 113 Kennedy Dr., Pangbourne,

Berks, RG87LD, England

Hydes, Paul C., 13 Woodlands Grove, Caversham, Reading,

Berks, RG4 ONB, England

Picker, Donald H., 310 Woodside Ave., Narbert, PA,

United States 19380

APPLICATION INFO: US 1900-0/3130 19000011 (6)

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on 27 Jun 1984, now abandoned

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DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
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NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 455

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Platinum co-ordination compounds comprising at least one amine ligand and a functional group remotely bonded to the amine ligand, which functional group may be linkable to a monoclonal antibody to provide a moiety which stabilizes the antibody against in vivo hydrolysis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 103436-53-9P

(prepn. and reaction of, with silver nitrate and hydrochloric acid)

RN 103436-53-9 USPATFULL

CN Platinum, amminediiodo(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

IT 103436-43-7P 103436-44-8P

(prepn. of, for linking to monoclonal antibodies, for drug delivery)

RN 103436-43-7 USPATFULL

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

RN 103436-44-8 USPATFULL

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are

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now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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